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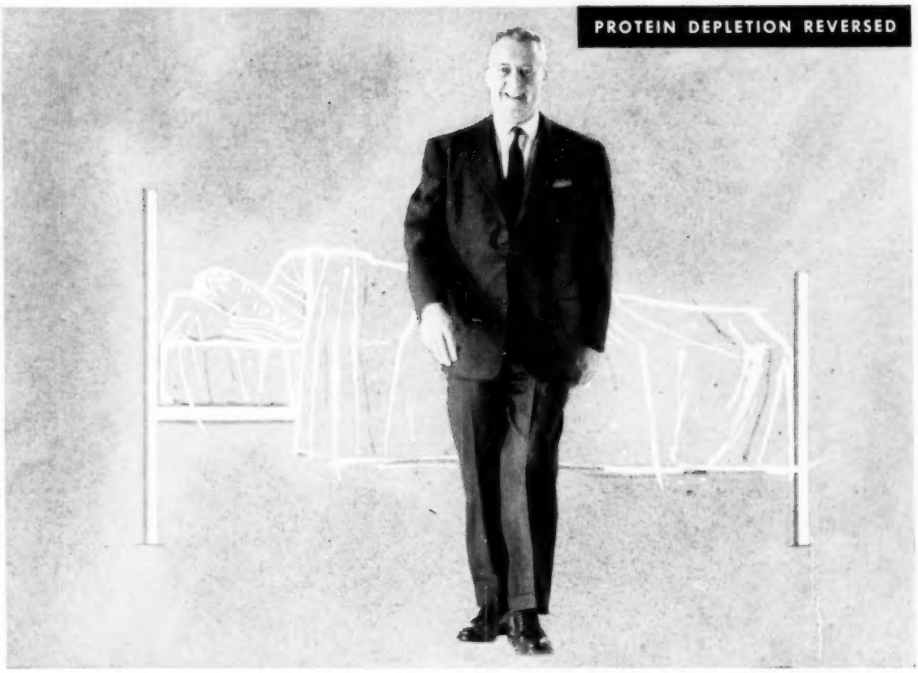

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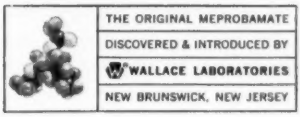

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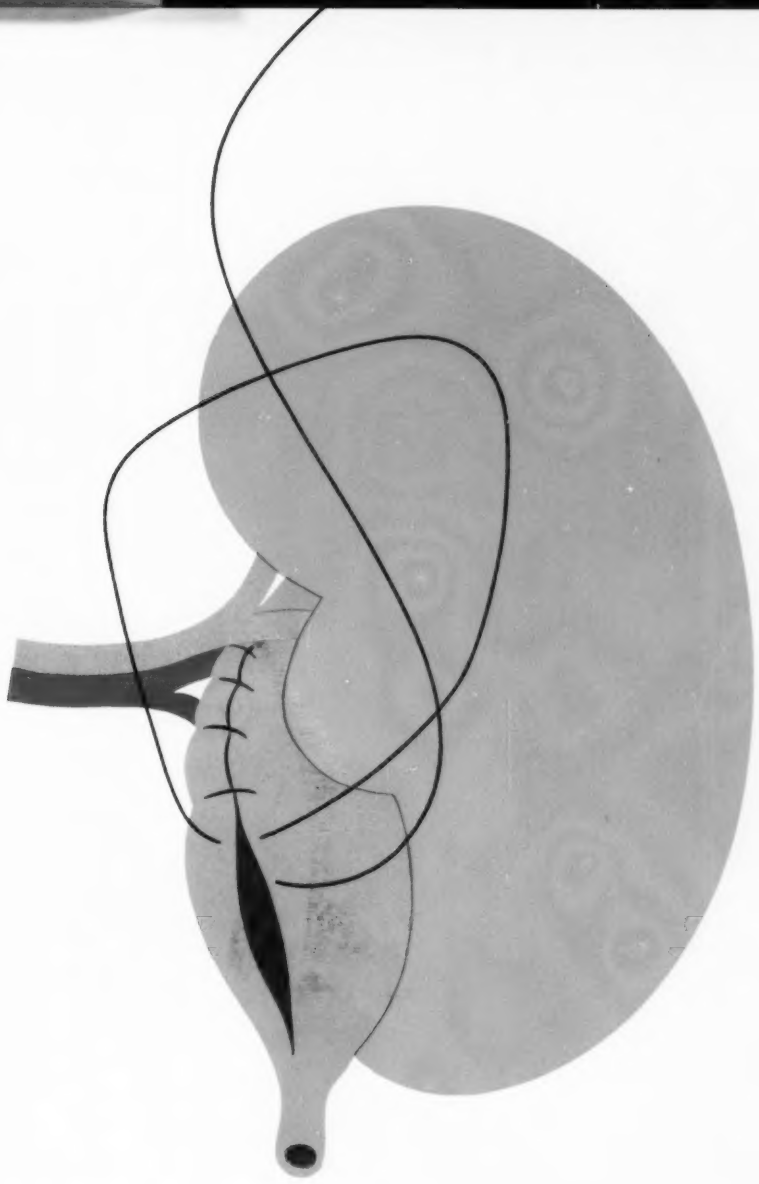

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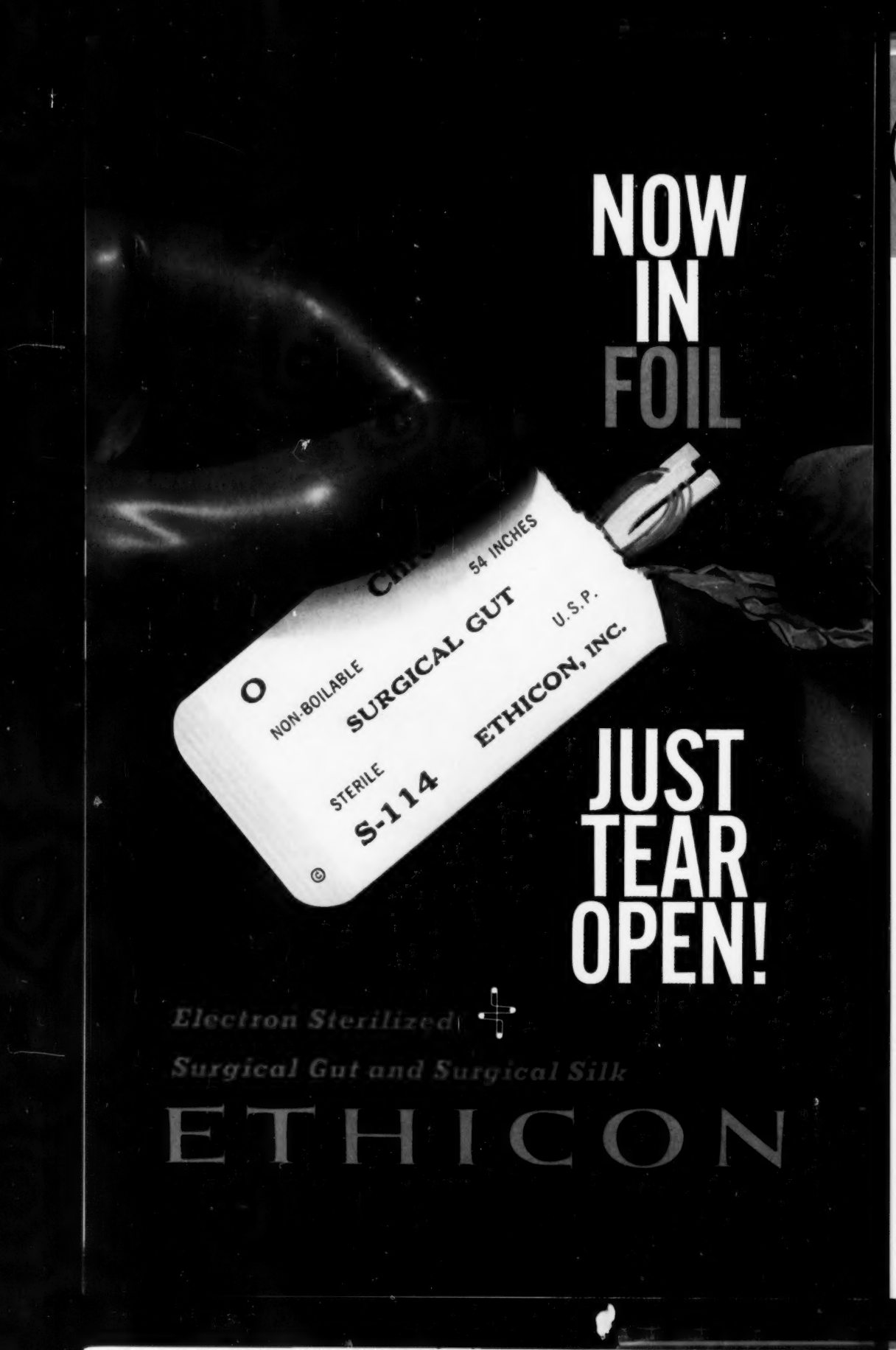
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Adrenalectomy for Hyperfunctioning Lesions of the of the Adrenal Cortex

EDWIN H. ELLISON, M.D., and GEORGE J. HAMWI, M.D., Columbus, Ohio

With the advent of adequate adrenal replacement and the development of a simplified anterior operative approach to the adrenals, total or subtotal adrenalectomy should rapidly become a standard procedure for many of the endocrine disorders resulting from hyperfunction or tumor of the adrenal gland. In turn, the modern surgeon will find it necessary to add the terminology of the adrenal physiologist and the endocrinologist to his fund of knowledge and to become familiar with a variety of adrenal hormones, including their mechanism of action and associated clinical phenomena.

This report is based upon cases reported in the literature and upon 12 cases in which operation was performed at Ohio State University Hospital from July, 1950, to August, 1957. The adrenocortical hyperfunction problems treated by total or subtotal adrenalectomy include eight cases of primary Cushing's syndrome, two cases of Cushing's syndrome secondary to pituitary tumor, one case of primary aldosteronism, and one case of congenital virilism associated with an adrenocortical carcinoma.

For the purpose of clarification, and since management depends upon etiology and the mechanism, when known, the lesions to be discussed have been categorized as (*a*) functioning tumors of the adrenal cortex, and (*b*) adrenocortical hyperfunction without tumor. Each of these categories is then subdivided into three disease entities according to the hormone secreted in excess: (1) Cushing's syndrome produced by excessive hydrocortisone; (2) aldosteronism produced by excessive aldosterone, and (3) virilism, produced by excessive adrenal androgens (Fig. 1). In cases of hyperfunction without tumor, each of these three major disease entities is further subdivided

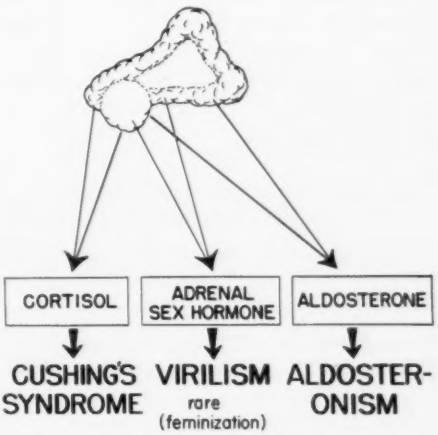

Fig. 1.—Diagrammatic sketch illustrating practical classification of endocrine disease entities of the adrenal gland. Note that functional tumors of the adrenal cortex and adrenocortical hyperfunction without tumor may be divided into three main groups, depending upon which of the three adrenal hormones is being produced in excess. Medullary hyperfunction has not been recognized clinically.

Read at the 65th Annual Meeting of the Western Surgical Association, Salt Lake City, Nov. 21, 1957.

From the Department of Surgery and the Division of Endocrinology of the Department of Medicine, the Ohio State University Health Center.

into primary and secondary, or, in the case of virilism, into acquired and congenital. Medullary lesions will not be discussed in this paper.

Functioning Tumors of the Adrenal Cortex

Cortical tumors may secrete excessive amounts of hydrocortisone and produce Cushing's syndrome,[1] or they may secrete excessive amounts of aldosterone, producing primary aldosteronism,[2] or they may secrete excessive amounts of androgens, resulting in virilism.[3] On rare occasions these tumors may produce excessive estrogens, resulting in feminization. Finally, tumors of the adrenal cortex may secrete any combination of these hormones, so that mixed syndromes, manifesting any or all of the clinical findings seen in Cushing's syndrome, virilism, or aldosteronism, may be present in any one case.

It is of interest that the majority of reported cases of Cushing's syndrome occurring prior to puberty were caused by tumor of the adrenal cortex and approximately 50% were malignant.

Although the etiology of tumors of the adrenal cortex remains unknown, two cases of congenital adrenal hyperplasia and associated virilization have recently been reported in which tumors were found after prolonged stimulation of the adrenal cortex by corticotropin U. S. P. (ACTH).[4,5]

Adrenocortical Hyperfunction Without Tumor

1. *Cushing's Syndrome.*—In a recent report by Plotz et al. 50% of the patients with Cushing's syndrome were dead within five years of the onset of the disease.[6] The seriousness of this disease process, therefore, is comparable to that of many common malignancies treated daily by the surgeon.

The etiology of adrenal hyperplasia with resulting Cushing's syndrome is still unknown. Some feel it is primarily a disorder within the adrenal cortex itself; others think it is probably a disorder of the pituitary

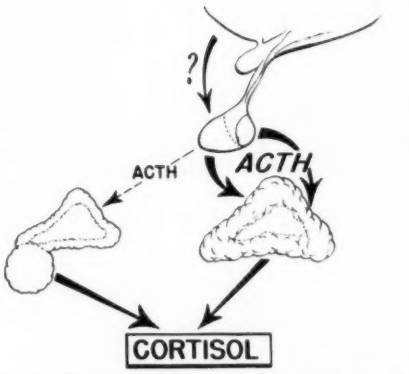

Fig. 2.—In tumors, the excessive secretions of hydrocortisone (cortisol) result in inhibition of the normal pituitary. Adrenocorticotropic hormone (ACTH) secretion is inhibited, and the contralateral and residual homolateral gland become atrophic. In hyperplasia, the primary derangement may be within the pituitary. In this instance the excessive adrenocorticotropic hormone secretion is unresponsive to the excessive hydrocortisone arising in the hyperplastic adrenals, and the vicious circle continues.

with excessive adrenocorticotropic hormone secretion[6] (Fig. 2). Still others postulate that it is the result of a disturbance in hypothalamic function, which, in turn, permits excessive adrenocorticotropic hormone secretion by the pituitary.[7,8] In the rare instance in which there is a discernible enlargement of the sella turcica, one must assume that the primary disorder resides within the pituitary.[9] This lack of knowledge regarding the etiology of Cushing's syndrome with bilateral adrenal hyperfunction without tumor is responsible for the variations in the approach to the control of this disease.

But, regardless of the etiology, Cushing's syndrome with adrenal hyperfunction is always associated with excessive hydrocortisone production. The major biologic actions of hydrocortisone include an increased ability to withstand stress, an anti-inflammatory action, an inhibition of tissue response to antigen-antibody reactions, the

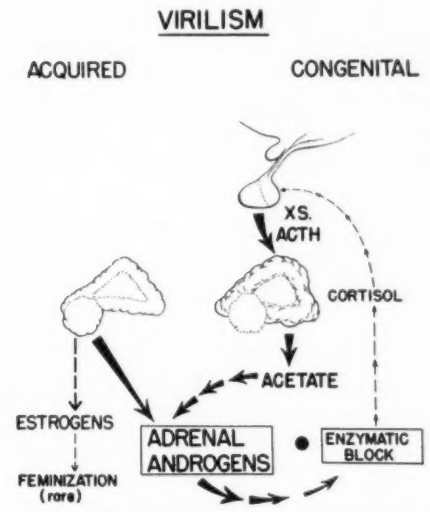

Fig. 3.—Diagrammatic sketch of mechanism involved in congenital adrenal hyperplasia and in virilism or feminization due to adrenal tumor.

ability to retain sodium and water and to excrete potassium, an increase in the excretion of calcium and phosphorus, and an inhibition of protein formation, with increased gluconeogenesis and fat mobilization and utilization.

Excessive amounts of hydrocortisone result in Cushing's syndrome, with the following symptoms, in the order of their occurrence: truncal obesity, hirsutism, hypertension, amenorrhea in females and impotence in males, plethora with purple striae, poor wound healing or infections, weakness and backache, purpura, acne, ankle edema, headache, neurologic symptoms, glycosuria with polydipsia or polyuria, virilism, and occasionally exophthalmos.

2. *Virilism.*—Prior to the availability of adequate replacement therapy, hyperplasia with virilism was treated by subtotal ad-

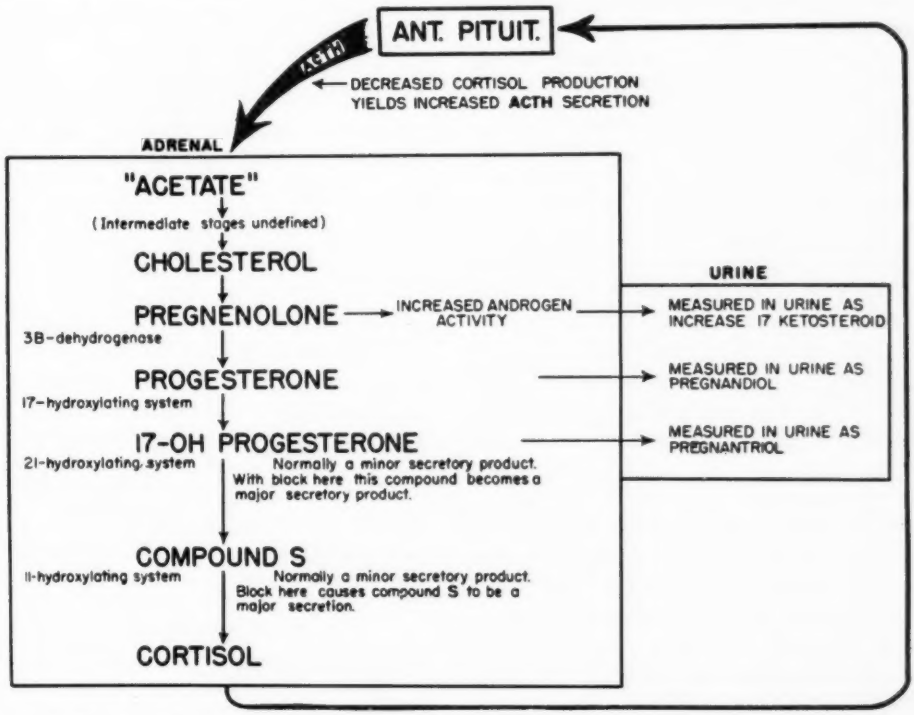

Fig. 4.—Chart illustrating normal metabolic sequence and the alterations in the various types of adrenogenital syndrome due to congenital adrenal cortical hyperplasia (After Hamwi). Reproduced from article by G. J. Hamwi, R. A. Serbin, and F. A. Kruger, published in the *New England Journal of Medicine* (257:1153, 1957) by the Massachusetts Medical Society, Boston.

renalectomy; however, the procedure was discontinued because of the large number of adrenal insufficiencies or inadequate resections, with subsequent hypertrophy of the remnant and recurrence of symptoms. Since that time the biologic mechanism resulting in congenital adrenal hyperplasia and masculinization has been defined [10] (Fig. 3). An enzymatic block demonstrated in congenital adrenal hyperplasia with virilism results in a deficiency of hydrocortisone, which normally inhibits the secretion of adrenocorticotropic hormone by the pituitary. Uninhibited production of this hormone stimulates the adrenal to produce excessive amounts of androgens (Fig. 4). Because the major abnormality is a deficit in the ability of the adrenal to secrete hydrocortisone, these patients are best treated medically by the administration of corticoids. The only role of surgery is the correction of congenital genital malformations.

Since the defect occurs in utero, the genital defects are apparent at birth and may make accurate determination of sex difficult. If the primary gonads in the fetus are ovaries, the result is a female pseudohermaphrodite with external genitalia simulating the sex opposite that of the primary gonads. Clinically, one may see a bifid scrotum, atrophic or absence of uterus, enlarged clitoris, and even hypospadias in extreme problems. If the defect occurs in a male fetus, precocious sexual development occurs, with an enlarged penis and pubic hair; however, the testes are small and rudimentary. In both sexes, the excessive androgens markedly stimulate skeletal growth, and therefore these children are initially larger and more muscular than normal children of equivalent age; however, the continued excessive secretion of androgens results in premature sealing of the epiphyses, so that growth ceases at a far earlier age than normal. The ultimate result is a short stature.

It should be noted that hirsutism may be present in conditions other than adrenocortical hyperfunction. This is particularly true of disorders of the ovary, such as arrhenoblastoma, adrenal-rest tumors of the ovary, and the Stein-Leventhal syndrome. In the absence of specific diagnostic tests, the only means of making a differential diagnosis is by actually visualizing the ovaries. The transabdominal approach at the time of adrenalectomy permits this and eliminates the possibility of a wrong diagnosis.

3. *Aldosteronism.*—Primary aldosteronism may result from cortical tumor or from adrenocortical hyperplasia [11] (Fig. 5). Since it is generally accepted that the secretion of aldosterone is only minimally dependent upon adrenocorticotropic hormone, surgical extirpation is the only treatment to be considered.

Aldosteronism presents a clinical picture of mild to moderate hypertension, intermittent episodes of weakness, high-normal or slightly elevated serum sodium, and, particularly, depressed serum potassium. Tetany may occur. Marked edema is not usually present.

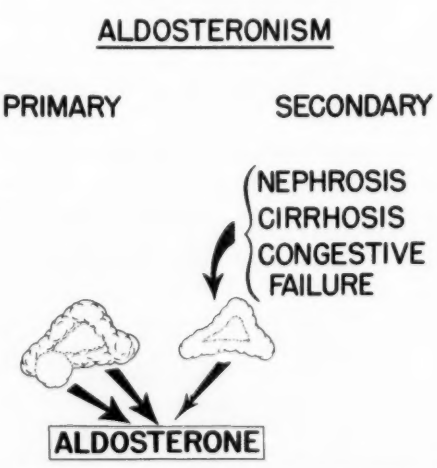

Fig. 5.—Diagram illustrating the two types of clinically recognized aldosteronism. The primary disease results from either hyperplasia or tumor of the adrenal gland. Secondary aldosteronism occurs after an increase in extracellular fluid volume and/or electrolyte imbalance.

LABORATORY DIAGNOSIS

	CUSHING'S		VIRILISM		ALDOSTERONISM	
	TUMOR	HYPERPLASIA	T	H	T	H
17 KETOSTEROIDS			MARKED INCREASE			
ACTH test CORT SUPP				+		
17 HYDROXYCORTICOIDS	MARKED INCREASE					
ACTH		+				
PREGNANTRIOL				INCREASE		
SERUM K+					MARKED DECREASE	

ADJUNCT PROCEDURES: I.V.P. CO_2 INSUFFLATION, AORTOGRAPHY

Fig. 6.—Summary of the laboratory diagnosis of Cushing's syndrome, virilism, and aldosteronism and the differentiation of cortical tumors from adrenocortical hyperfunction without tumor. In aldosteronism, the adjunct procedures of intravenous pyelography, CO_2 insufflation, and aortography are the only methods available to assist in the diagnosis of tumors of the adrenal cortex.

Laboratory Diagnosis of Cortical Hyperfunction

The laboratory diagnosis of adrenocortical hyperfunction is presented in Figure 6. Steroid determinations are not absolute, and measurements of 17-ketosteroids and of 17-hydroxycorticosteroids (hydrocortisone) in the urine are actually estimates of groups of substances having varying biologic activities. Normal values must be established by each laboratory; therefore no values are reported in the chart.

In Cushing's disease there is a marked increase in both the plasma and the urinary levels of hydrocortisone.[12] Stimulation with corticotropin will cause little or on effect if the excessive secretion is due to tumor. If the primary disturbance is bilateral adrenal hyperplasia, there will be more than the usual threefold increase in the level of plasma hydrocortisone following a six-hour intravenous infusion of 25 mg. of corticotropin and an appreciable increase in urinary hydrocortisone (corticotropin test). In Cushing's disease, glucocorticoids do not suppress hydrocortisone secretion.

In patients with manifestations of virilism, laboratory tests are helpful in differentiating hyperplasia from tumor, but are not absolute.[5] In virilism due to adrenal tumor the urinary 17-ketosteroids are markedly elevated and are not suppressed by glucocorticoids. In virilism due to adrenal hyperplasia, there is a prompt and dramatic drop in the level of urinary 17-ketosteroids following the suppression of adrenocorticotropic hormone of the anterior pituitary by fludrohydrocortisone (6 to 8 mg. per day). Stimulation with corticotropin does not appreciably alter the level of 17-ketosteroid excretion in cases of adrenal tumor; however, the administration of corticotropin results in a marked increase in the 17-ketosteroid excretion in hyperplasia, but little or no increase in the hydrocortisone (17-hydroxycorticosteroid) excretion, since the enzymes necessary to form hydrocortisone in the adrenal gland are absent. Finally, elevated levels of urinary pregnanetriol indicate congenital adrenocortical hyperplasia.

Laboratory tests for the determination of aldosterone are still exceedingly difficult and are usually available only at medical centers performing investigative work in this area. From the clinical point of view, primary aldosteronism should be suspected when serum potassium levels are persistently lowered and no other cause can be found.

It should be noted that there is no reference in the chart (Fig. 6) to ancillary or indirect tests of adrenocortical function, such as the eosinophil count, uric acid-creatinine ratio, or glucose tolerance. These have proved to be of little or no diagnostic value, in spite of their physiological interest.

Adjunct Diagnostic Studies

Since cortical tumors usually exert pressure on the medial aspect of the upper pole of the corresponding kidney, lateral or inferior displacement of the kidney may be seen in a plain K. U. B. x-ray or with an intravenous pyelogram (I. V. P.). In addition, elongation and displacement of the upper major calyx may occur. Presacral CO_2 insufflation under local infiltration anesthesia may prove diagnostic in the absence of kidney displacement. A normal adrenal gland is not visualized by this procedure, and the kidney outline is not dis-

torted. The finding of a well-demarcated mass on the upper pole of the kidney is very suggestive of adrenal pathology. On occasion, one may differentiate hyperplasia from tumor by the demonstration of lobulation. Aortography may be useful if all other studies fail to prove the presence of a suspected tumor. The finding of increased vascularity or the demonstration of abnormal or distorted vessels suggests the presence of tumor. Aortography and CO_2 insufflation are contraindicated if a pheochromocytoma is suspected.

Preoperative Preparation

It is generally accepted that the abnormalities and physiological alterations in Cushing's syndrome are the direct result of excessive hydrocortisone production. The primary aim of treatment, therefore, is to reduce the level of corticoid production; however, sudden lowering of the available corticoids by adrenalectomy may result in adrenal insufficiency during operation or in the immediate postoperative period if the patient is not preoperatively prepared.

The simplest method of preparation is the administration of cortisone acetate, 100 mg. I. M. every 12 hours for four doses, the last dose being given immediately prior to operation. Since cortisone acetate is a suspension of crystals, and is absorbed only gradually from the site of injection, adequate blood levels are maintained.

Intravenous substitution therapy with hydrocortisone hemisuccinate or fludrohydrocortisone, starting with the onset of anesthesia, may also be used, but is far more complex, owing to the mechanical difficulties of maintaining continuous intravenous administration and adjusting the rate of flow. Also, there is rapid loss of effect once the intravenous source is discontinued, since the half-life of cortisone in blood is 110 minutes. Intravenous administration is of greatest value as a supplement to the intramuscular Depo-Cortisone if one suspects inadequate absorption or too small a reserve of corticoids.

Serum potassium deficits, if present, should be corrected preoperatively by the administration of oral potassium salts.* Some physicians recommend correction of marked protein depletion by preoperative administration of testosterone. This is only partially effective and requires fairly prolonged administration before any appreciable anabolic effect is obtained. It seems wiser to remove the cause of excessive catabolism by surgically removing the adrenal glands, rather than prolong the preoperative period. Finally, since one of the serious potential complications of excessive corticoid activity is a decreased resistance to infection, it is felt advisable to use prophylactic antibiotic therapy.

The preoperative preparation is the same whether the Cushing's syndrome is resulting from hyperplasia or tumor.

Operative Approach to Adrenalectomy

The operative approaches to the adrenal glands are many and varied [13,14]; however, the following criteria must be met. First, and most important, the surgeon must be able to visualize both of the adrenal glands *before* deciding upon the definitive operative procedure.[15] Second, he should be able to explore the ovaries for disease simulating cortical hyperfunction or tumor.[16] Finally, the sites of cortical rests should be examined for aberrant adrenal tissue. The only procedure found to meet all of these criteria is the anterior transabdominal approach, which permits exposure of all adrenal tissue, including sites of cortical rests, as well as exploration for ovarian disease. The technique for sufficient mobilization to permit adrenalectomy under direct vision, the key to this procedure, will be presented in a future paper.

Total Versus Subtotal Adrenalectomy

Severe hypertension, as indicated by the presence of cardiac enlargement, is our sole

* Warren-Teed Products Company furnished supplies of Kaon, containing potassium gluconate (5 ml. is equivalent to 0.5 gm. KCl).

indication for total adrenalectomy, since in these instances even a small remnant will result in the maintenance of the hypertension.[17] Three of our ten patients with Cushing's disease met this criterion, and in these cases the blood pressure returned to normal in each instance (Cases 1, 2, and 9).

It should be remembered that cortisone replacement therapy is vital following total removal of the adrenal glands and that total replacement therapy for the remainder of the patient's life is exceedingly troublesome and expensive.

When subtotal removal of adrenal tissue is indicated, left total and right subtotal adrenalectomy is preferred, with sufficient amounts of the gland removed to control the mainfestations of hypersecretion, yet with sufficient residual function to maintain optimum physiological activity.[18]

A satisfactory estimate of the size of the remnant may be determined by comparing the weight of that portion removed with the total weight of the contralateral gland. In our experience, a left total adrenalectomy combined with a 60% to 70% removal of the right adrenal is sufficient to control cortical hyperfunction without the need for replacement therapy. The one patient with an 84% resection (Case 5) required cortisone replacement equivalent to that required by patients with total adrenalectomy. On the other hand, the one patient with a 50% resection (Case 8) failed to respond and required subsequent re-resection to control the disease process. Further experience may enable us to develop a more accurate rule of thumb.

Precautions During and Following Operation

If the patient has sufficient corticoid reserve, anesthesia presents no particular problems other than those associated with obesity. Bony injury secondary to the marked osteoporosis may be a problem and certainly should be kept in mind when moving or positioning the patient.

Meticulous attention to hemostasis before closure and careful approximation of the surgical incision are essential because of the abnormal bleeding tendencies and poor wound healing manifested by these patients.

Hypotension and a rising pulse rate occurring soon after the induction of anesthesia may indicate an unsuspected chronic shock, wherein a depleted blood volume has been masked by an increased red cell mass, seen frequently in Cushing's syndrome. In this instance, whole blood, plasma, or albumin is indicated.

The differential diagnosis and proper treatment of hypotension occurring during or immediately after operation constitute a major problem. Adrenal insufficiency must always be considered when hypotension occurs which is inconsistent with blood loss. The pulse rate usually remains unchanged in early adrenal insufficiency. It should be remembered that patients receiving or recovering from cyclopropane frequently have a slow pulse in the presence of hemorrhage. Active blood loss, therefore, must be considered when unexplained hypotension occurs early in the postoperative period in patients with a normal pulse rate. A deficiency of hydrocortisone may be differentiated from cyclopropane shock by infusing very small amounts of a vasopressor (5 mg. of phenylephrine hydrochloride U. S. P. [Neo-Synephrine] in a liter of 5% dextrose) by slow intravenous drip, which method should control the hypotension resulting from cyclopropane within a short time. If the blood pressure has not returned to normal by the time 100 cc. has been injected, the possibility of adrenal insufficiency must be considered. In this instance, 100 mg. of hydrocortisone acetate in 10 cc. of sterile water is infused in divided doses over a 12-minute period (25 mg. every three min. for four doses). If the blood pressure responds, hydrocortisone is continued by slow intravenous drip.

Postoperative Replacement Therapy

Cortisone substitution therapy in the immediate postoperative period is the same

following removal of a unilateral cortical tumor as following total or subtotal resection for cortical hyperfunction. In each instance 100 mg. of cortisone acetate is given intramuscularly every 12 hours for two days. Oral cortisone in equivalent doses may be substituted for intramuscular cortisone acetate when tolerated.

The need for continued replacement varies with the type of cortical hyperfunction and the extent of resection of adrenal tissue. Total adrenalectomy presupposes complete adrenocortical replacement for the duration of the patient's life. In our experience, optimum replacement in the absence of severe hypertension includes adequate provision of desoxycorticosterone acetate U. S. P. to maintain normal serum electrolytes. In the immediate postoperative period a daily intramuscular injection of 2 mg. of desoxycorticosterone acetate (DOCA) is sufficient. Following recovery, subcutaneous implantation of two 75 mg. DOCA pellets constitutes effective electrolyte hormone replacement therapy for 8 to 12 months. With this replacement, smaller doses, of 20 to 30 mg., of oral cortisone for each 24-hour period are usually adequate to maintain patients with total adrenal insufficiency. It must be remembered that the maintenance dose of cortisone must be increased whenever the patient is faced with a stressful situation.

Since the adrenal glands are the only significant source of androgenic hormones in females, replacement is necessary following total adrenalectomy. Experience has shown that replacement therapy improves the patient's mood and general strength. Two 75 mg. pellets of methyltestosterone implanted simultaneously with the DOCA pellets will assure sufficient androgens for three to four months. Methyltestosterone is then given orally in a dose of 10 mg. per day until such time as additional DOCA pellets are implanted.

If a functioning unilateral cortical tumor has been removed for relief of Cushing's syndrome, the contralateral adrenal cortex is probably atrophic and must always be stimulated with corticotropin before cortisone substitution therapy is discontinued. The intramuscular injection of 40 units of a long-acting corticotropin preparation every 12 hours for a minimum of four days prior to complete withdrawal of the replacement cortisone is an adequate precaution against adrenocortical insufficiency in most instances. Inadequate priming results in the usual picture of weakness, asthenia, epigastric distress, postural hypotension, headache, and, eventually, collapse. If this symptom complex is seen, corticotropin therapy should be reinstituted for several more days. The ultimate measure of the adequate response of the residual adrenal cortex is the finding of normal urinary or plasma levels of hydrocortisone without corticotropin stimulation.

Contralateral cortical atrophy is also present in approximately one out of three cases of virilism associated with a unilateral cortical tumor; therefore similar precautions are required. Since primary aldosteronism resulting from a cortical tumor has no effect on the normal adrenal cortex, corticotropin stimulation is not necessary before withdrawing cortisone.

Problems related to cortisone withdrawal following subtotal adrenalectomy for hyperfunction without tumor may be troublesome initially, due to the difficulty of ascertaining the functional capacity of the adrenal remnant after the marked inhibition produced by the vigorous attempt to assure an adequate cortisone reserve during the stress of operation and the immediate postoperative period. To date, the method of continued gradual reduction of cortisone replacement from the dose level of 50 mg. per day, supplied on the fifth and sixth postoperative days, together with close observation for clinical manifestations of adrenal insufficiency, is the only practical method of determining residual function.

An asymptomatic patient with normal plasma hydrocortisone probably has an adrenal remnant functioning sufficiently to

meet the usual requirements of hospital life. But will this same adrenal remnant prove sufficient when the patient returns to his home and is once again faced with even the minor problems of everyday living? Adrenalectomy patients must be watched closely during the first 12 months of convalescence lest the physician overlook intermittent and mild clinical evidence of chronic adrenal insufficiency, which a minor stressful situation may make acute and life-endangering. Mild, almost subclinical cortical insufficiency was recognized in two of our patients. In the patient operated on for Cushing's syndrome (Case 5), the symptom complex improved rapidly after the intramuscular injection of hydrocortisone. The second patient, operated on for primary aldosteronism (Case 11), whose plasma and urinary steroids had remained at the lower limits of normal, experienced several episodes of acute adrenal insufficiency, associated with an increased intracranial pressure and bizarre CNS symptoms, classified as metabolic craniopathy. Moderate cortisone replacement eliminated these acute episodes and has resulted in marked improvement in her general health, including a 10-15 lb. weight gain. It is strongly suggested that the long-term follow-up of these patients be entrusted only to those physicians who are well acquainted with adrenocortical hypofunction.

Clinical Results

The clinical picture, laboratory findings, operations, pathology, and long-term results of our patients with Cushing's syndrome, aldosteronism, and virilism associated with an adrenocortical tumor are presented in the accompanying Table.

All eight of the patients with primary Cushing's syndrome are living and well. The time since operation varies from 3 months to 5 years, with an average interval of 22 months. The age at operation ranges from 7 to 52 years. Of the six subtotal adrenalectomy patients in this group, one required the removal of additional adrenal tissue for persistence of symptoms, and a second required replacement therapy. Two patients underwent successful total adrenalectomy. Three of the eight patients developed postoperative complications worthy of mention: paralytic ileus in one, atelectasis in two, and infections in two. Six of the eight had preoperative systolic pressures greater than 150 mm. of Hg or diastolic pressures exceeding 100 mm. Five of the six are now normotensive. Preoperative blood pressures in the two total adrenalectomy patients were 225/142 and 180/120, respectively; both are now normotensive.

The one operative death in the series (Case 10) resulted from hemorrhage secondary to an abnormal clotting mechanism in one of the patients with a primary pituitary tumor. The second patient with a pituitary lesion (Case 9) responded well to subtotal adrenalectomy but died some two months later, following a reaction to a splanchnic block.

Several months following subtotal adrenalectomy, the one patient with aldosteronism developed increased intracranial pressure, which responded to ventricular taps and eventually to cortisone replacement. The significance of these observations will be published later.

The patient with virilism and an adrenocortical tumor menstruated for the first time several months ago; her body contour is more feminine, and her general well-being is excellent. To date, there is no evidence of recurrence of the malignant cortical tumor.

Summary

1. A practical classification of disease entities resulting from functioning cortical tumors or adrenocortical hyperfunction without tumor is presented.

2. The clinical syndromes resulting from excessive amounts of hydrocortisone, (cortisol), aldosterone, and adrenal androgen are described, and the methods of diagnosis and management are suggested for each.

Diagnosis	Case No.	Age	Sex	Race	Predominant Findings	Duration of Disease	Pertinent Laboratory Findings			Positive X-ray Findings
							17-Keto., Mg/24 Hr.	17-OH., Mg/24 Hr.	Other	
Cushing's Syndrome (primary)	1	48	F	W	Girdle obesity; 102 lb. wt. gain; marked fatigue; bruised easily; mild hirsutism; B. P. 170/92; enlarged heart	5 yr.	23.1–25	3.4	Red cell mass +380 cc.; coag. time 12′ 22″	Slight osteoporosis; adrenals seem enlarged by aortography
	2	39	M	W	Severe headaches; one episode of cardiac failure; B. P. 225/142; enlarged heart; moon face; ruddy complexion; purple striae; prominent eyes; bilateral rib fractures	2 yr.	4.6–16.3	15.2–34.8	Serum Na, 151 mEq.; red cell mass + 950 cc.	Enlarged heart; bilateral rib fractures; normal CO_2 insufflation
	3	7	M	W	Increased appetite and obesity; irritability; pubic hair; development of external genitalia; purplish striae; acne; puffy, livid face; B. P. 170/90; wt. 86 lb.	16 mo.	16.5–18.8	19.7–54.8	Serum Na, 149 mEq; corticotropin test +; WBC 17,700	Normal aortogram; bony development age 4 yr.
	4	25	F	W	Amenorrhea; lack of ovulation; 30 lb. wt. gain; B. P. 114/70; large; tender breasts; trunkal obesity	3 yr.	12.1–17.0	19.5–27.5 plasma, 28.9	Serum Na; corticotropin test ?	None—normal sella turcica
	5	26	F	W	Progressive hirsutism; 70 lb. wt. gain to 194 lb.; trunkal obesity; amenorrhea; B. P. 122/82; bulging eyes, striae, acne	2 yr.	20.5–46.7	43.7–70.4	Plasma 17-OH. increase from 27 to 76 mg. % with corticotropin	None—normal sella turcica
	6	26	M	W	Wt. gain with trunkal & facial obesity; striae, plethora; B. P. 150/104; wt. 167 lb.; weakness, dizziness & fullness in head; recurrent renal stones 4 yr.	4 yr.	14.7–27.7	11.1–33.8	Plasma 17-OH. incr. from 21.2 to 90.9 mg. % with corticotropin	Minimal cardiomegaly anterior wedging lumbar spine
	7	52	F	W	Wt. gain to 294 lb. with hirsutism since birth of 1st child; amenorrhea; diabetes; B. P. 180/96; striae, moon face, coarse & thinning hair	36 yr.(?)	6.8–10.7	8.7–20.9	Serum Na, 148 mEq.; equivocal corticotropin test	Superior pole left kidney displaced to left; osteoporosis
	8	20	F	W	Patient's wt. gain during pregnancy, 7 mo. previously; amenorrhea since delivery; acne, striae, weakness, blurring of vision; B. P. 160/120; moon face, trunkal obesity, facial hair	1 yr.	13.3–53.4	34.5–93.2	Blood vol. deficit 1390 cc.; serum Na, 149 mEq.; K, 2.1 mEq.; plasma 17-OH. 25.4to 126.9 mg. % with corticotropin	Normal
Cushing's syndrome (secondary to pituitary tumor)	9	27	M	W	Wt. gain since puberty; gynecomastia; marked fungus infection; lost 2″ in ht.; paroxysmal nocturnal dyspnea, blurring of vision, chest pain, nocturia; X's 3; B. P. 200/130; small genitalia, pitting edema, marked hyperkeratosis	14 yr.	8.0–38.2	11-desoxy. 1.2– 1.9	Bleeding time, 4′ 35″; prothrombin 52.5%; serum Na, 152 mEq.; K, 2.8 mEq.	Marked osteoporosis with 2 collapsed vertebrae; sella turcica normal
	10				Weakness & fatigue, impotence, moon face; striae; hypertension B. P. 180/90; multiple ecchymosis & petechiae; palsy of cranial nerves 3, 4, & 6; all recurrent 1.5 yr. after hypophysectomy & insertion of cobalt	3.5 yr.	42.0	3.0– 3.4	Blood clotting time normal; prothrombin 120%	Sella turcica 26×16×8 mm.; heart enlarged 18%; duodenal ulcer
							11.8	18.7	Negative corticotropin test	Cardiac hypertrophy; mult. healed rib fractures

Hyperfunction—Case Summaries

Operation Date	Surgical Pathology: Microscopic	Adren. Wt., Gm. Rt.	Adren. Wt., Gm. Lf.	Postoperative Complications	Results: Time Since Operation	Replacement	Comments
Bilateral total adrenalectomy, splenectomy, liver & lymph node biopsy 11/17/52	Hyperplasia of vesicular layer	7.8	8.0	Left basal pleural reaction; temporary adrenal insuffic	5 yr.	DOCA pellets q. 8 mo.; prednisone, 5 mg. b. i. d.; slight pigmentation	17-keto., 2.7 mg/24 hr.; 17-OH, 1.3–2.4 mg. B. P. 120/90; Cushing's syndrome controlled
Bilateral total adrenalectomy 5/15/57	Cortical hyperplasia with small nodules of cortical tissue	11.5	12.0	Wound abscess	6 mo.	Cortisone 12.5 mg. t. i. d.	B. P. 140/90; no evidence of failure; Cushing's syn. controlled; serum Na, 139 mEq.
Left total adrenalectomy, right subtotal adrenalectomy 10/5/54	Probable hyperplastic changes in cortex; marked vaculation	3.5	7.0	Paralytic ileus; L. L. L. atelectasis	3 yr. 1 mo.	None	17-keto., 1.5–3 mg/24 hr.; 17-OH, 6.1–13 mg/24 hr.; wt. to 57 lb., with normal development; marked pigmentation; B. P. 100/80; marked increase in activity
Left total adrenalectomy, right subtotal adrenalectomy, cf ovaries, appen. 12/6/56	Normal	4.0	7.0	None	11 mo.	None	Normal menstruation but unable to conceive; remains obese; normal steroid production, negative corticotropin test
Left total adrenalectomy; right subtotal adrenalectomy; ovarian biopsy 8/21/57	Normal	6.3	7.5	None	3 mo.	DOCA implants cortisone 37.5 mg/day	Plasma 17-OH., 3.24 mg.% with no response to corticotropin; Cushing's controlled but adrenal insufficiency requires replacement
Right total adrenalectomy; left subtotal adrenalectomy 6/19/56	Cortical hyperplasia; fasicular layer wider, with cells rich in lipid content	10	7	None	1 yr. 5 mo.	None	Cushing's controlled syn.; no insufficiency with 2 operations for ureteral stone
Left total adrenalectomy; biopsy of ovaries 8/25/55	Diffuse hyperplasia of adrenal cortex with large amount of lipid	--	4	Minimal L. L. L. atelectasis	2 yr. 2 ½ mo.	None	Minimal changes; developed adenocarcinoma of uterine endometrium 1 yr. postadrenalectomy; treated with radio active cobalt
Left total adrenalectomy; right subtotal adrenalectomy 4/24/56	No significant change	4.5	7.5	Hypokalemic, hypochloremic alkalosis	4 mo.	None	Persistent symptoms, including severe headaches & blurring vision; positive ACTH test
re-resection rt. adrenal 8/5/56	Cells hyperplastic with 1 gm. lipid content	?		None	1 yr. 7 mo.	None	Cushing's syn. controlled; plasma 17-OH., 11.5 mg.%
Bilateral total adrenalectomy, appendectomy 7/30/51	½ mm. nodules in each cortex	5.6	5.4	Initial adrenal insufficiency; cystitis; perirectal abscess	41 days	Cortisone 25 mg. 2–4 X's/day	Patient died suddenly on 41st postoperative day, following splanchnic block; prior to this Cushing's syn. controlled & keratotic skin desquamated; pituitary tumor & cyst at autopsy
Hypophysectomy, insertion of radioactive cobalt 9/17/52	Chromophobe			Hemorrhage from duodenal ulcer	2 yr. 4 mo.	None	Symptoms recurred 1.5 yr. following hypophysectomy
Bilateral total adrenalectomy 5/25/55	Normal appearance	6	4.8	Massive retroperitoneal bleeding, uncontrolled by reoperation	1 day	Hydrocortisone	Patient died of postoperative bleeding; recurrent tumor at autopsy

Diagnosis	No.	Age	Sex	Race	Predominant Findings	Duration of Disease	Pertinent Laboratory Findings			Positive X-ray Findings
							17-Keto., Mg/24 Hr.	17-OH., Mg/24 Hr.	Other	
Aldosteronism (primary)	11	49	M	W	Wt. gain of 25 lb.; facial hirsutism, ankle edema, dysmenorrhea, & menorrhagia; spontaneous ecchymosis; periorbital edema; cardiac enlargement; B. P. 190/100	5 yr.	15.6	11.1–17.0	Serum Na, 151 mEq.; K, 3.1 mEq. Equivocal corticotropin test	Healing fracture left 5th rib; sella turcica border line enlargement; I. V. P. normal
Congenital virilism (with nonfunctioning adrenocortical carcinoma)	12	39	F	C	Facial hair requiring shaving since age of 9 yr. amenorrhea; male body build; hypertrophied clitoris amputated in 1943; small, atrophic uterus & ovaries; small breasts; family history of similar problems in 3 sisters	39 yr.	106.3–117.3	9.5–18.1	Serum Na, 147 mEq.; 17-keto. from 106.3 to 205.7 with cortieotropin & desc. with fludrocortisone; pregnanetriol markedly elevated	Air insufflation normal in 1943; tumor mass displacing left adrenal by I. V. P. & CO_2 insufflation at this admission

3. Preoperative management and the rationale for the anterior transabdominal approach to adrenalectomy are presented.

4. The results in the 12 cases in which operation was done at University Hospital are reviewed.

University Hospital, Ohio State University College of Medicine.

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Hyperfunction—Case Summaries—(Continued)

Operation Date	Surgical Pathology: Microscopic	Surgical Pathology: Adm. Wt., Gm. Rt.	Surgical Pathology: Adm. Wt., Gm. Lf.	Surgical Pathology: Postoperative Complications	Results: Time Since Operation	Results: Replacement	Results: Comments
Left total adrenalectomy, right subtotal adrenalectomy; removal uterine fibroid, oophorectomy 8/16/55	Nodular hyperplasia of cortex grossly & microscopically; cortical cells rich in lipid; fibroid, atrophic ovary	4.7	9.7	Minimal atelectasis	2 yr. 3 mo.	Prednisone 5 mg. t. i. d.	17-keto. 1.3–7.7 mg/24 hr.; 17-OH., 3.9–9.8 mg.; 1 episode of cerebral edema (metabolic craniopathy), like water intoxication; responded to cortisone, ? XTSH production with thyrotoxicosis
Left total adrenalectomy, including resection of large malignant cortical adenoma of left adrenal 2/1/57	Well-differentiated adrenocortical carcinoma, infiltrating fat & lymph nodes; no normal adrenal identified	228	228	None	9 mo.		Steroid excretion, corticotropin stimulation, & cortisone suppression unchanged; all controlled with cortisone (Does prolonged X's corticotropin play role in adrenocortical tumors?)

DISCUSSION

Dr. Arthur Jesse Hunnicutt, Oakland, Calif.: In the past four years I have had the good fortune to have experience in 16 cases of this type. Three tumors were functioning adenomas (Cushing). In six cases I did a subtotal adrenalectomy (masculinizing, salt retention, and Cushing's syndrome in three, total adrenalectomy (hypertension). In two cases the adrenals and ovaries were normal (hirsutism). In five cases the adrenals were normal, and the only findings were the so-called polycystic ovaries, or the Stein-Leventhal syndrome.

I should like to emphasize what Dr. Ellison has brought out, that the transabdominal approach to these problems is preferable, for the reasons he has stated. I would like to go one step further and emphasize the importance of looking not only in the adrenal area but in the rest of the retroperitoneal area, where adrenal tissue may be.

I expose the adrenals in essentially the same way, except that I do not cut the gastrocolic omentum. There are two embryonic layers posteriorly: one, the gastrointestinal tract, and the other, the urinary tract. Freeing the colon in front of the kidney, with the dissection carried superiorly on the left side, puts one behind the spleen, pancreas, and stomach; all are reflected up anteriorly. This dissection is anterior to the kidney.

The second point, which has been very helpful, is that of dissecting, posterior to the kidney, the second embryonic layer and carrying the dissection by hand superiorly, behind the adrenal. Thus the kidney acts as a "handle." One can turn the left adrenal up into the abdominal wound, and one does not have to touch the adrenal. One can do the same on the right side, but not quite as conveniently.

The second reason for going behind the kidney, and, in turn, carrying the dissection inferiorly, behind the ureter, is that one can visualize the sympathetic ganglia to the pelvis.

One point on the subtotal adrenalectomy: I have never heard a satisfactory definition of a subtotal adrenalectomy. A subtotal adrenalectomy as defined by Dr. Ellison, we have found, is inadequate. It is not how much is taken out, but what is left, that is going to affect the patient. We have been leaving at the right upper pole a triangular piece of adrenal tissue about 1.5 cm. across. These patients will require steroid support for a few months.

I should like to ask Dr. Ellison whether he has had to go back in and take out more adrenal tissue.

Dr. D. Emerick Szilagyi, Detroit: I want to express my great appreciation to Dr. Ellison for a clear and concise presentation of a complex problem.

I arise mainly to call your attention to aldosteronism, a most interesting disease, first described by Dr. Jerome Conn, of Ann Arbor. His description of this entity was a striking example of sound deductive reasoning. By knowing the hormone aldosterone and its characteristics, and then fitting these facts into a pattern, he made the diagnosis in a clinical case the features of which up to then had been entirely obscure. Before the work of Conn, aldosteronism—characterized principally by sodium retention, excessive potassium excretion, and hypertension—had been diagnosed in most cases as a form of nephrosis.

We had an opportunity to operate on a 12-year-old Negro boy with aldosteronism. We found that the cortex of both adrenals was markedly hyperplastic but there was no tumor formation. In

microscopic sections the hyperplasia appeared to be localized in the zona glomerulosa of the cortex. Bilateral total adrenalectomy brought complete relief of the metabolic aberrations for at least four months.

It is very possible that in the future we shall see many more cases of this type.

Dr. Edwin H. Ellison, Columbus, Ohio: In answer to Dr. Hunnicutt's question regarding the extent of adrenal resection versus the necessity of steroid replacement: It has been our experience that patients requiring steroids during the first few months will require replacement for life. However, this would not hold true of patients who had been exposed to abnormally stressful situations during this period.

In animals, ligation of the veins from the adrenal gland with the arterial supply intact results in atrophy. This fact may explain the high percentage of atrophy and resultant adrenal insufficiency reported by Dr. Hugh Young following subtotal resection for virilism. The unfavorable results led him to give up the procedure. We have attempted to preserve sufficient functioning tissue so that the patient would not require steroids for life.

In our experiences to date, total removal of one adrenal gland, combined with a 60% to 72% resection of the opposite adrenal gland, has proved sufficient to control the excessive function without the need for replacement therapy. Reoperation was required in the one patient with a 50% resection included in the series. In the one patient with an 84% resection of the second adrenal, steroid replacement is still necessary. In effect, therefore, the patient has had a total adrenalectomy.

It is very interesting that Dr. Szilagyi has seen adrenal hyperplasia with aldosteronism. To the best of my knowledge, there are only two reported cases in the literature, including the one we have present today.

Prognosis in Peripheral Arterial Insufficiency Associated with Claudication or Ulceration

HERBERT J. ROBB, M.D.; JOHN W. BOWDEN, M.D.; RUDOLPH CASTELLANI, M.D., and CHARLES G. JOHNSTON, M.D., Detroit

Many studies have been reported concerning the effectiveness of sympathectomy in peripheral arterial insufficiency. The results have been variable since the early studies by Harris,[6] Leriche,[8] and Atlas.[1] Most of these have dealt with changes following sympathectomy and the end-results. In the present study we have surveyed our cases with symptomatic peripheral arteriosclerosis, primarily to determine factors which might be useful in estimating prognosis. These factors, incorporated in a simplified classification, make it possible to estimate the probability for improvement in walking ability, amputation, or death.

One hundred forty patients with symptomatic peripheral vascular occlusive disease were selected for study at the Dearborn Veterans' Administration Hospital. Those with frostbite, phlebitis, or embolus were not included. These patients had received the benefits of all available medical and surgical therapy except use of the arterial homografts. The course of each patient was reviewed on an average of three years following lumbar sympathectomy, the last sympathectomy in the series having been done in December, 1955.

During the study, information was acquired concerning the following factors: age of patient, duration of symptoms, presence of diabetes, claudication, ulceration, amputation rate, longevity, and indications for lumbar sympathectomy. A special effort was made to compare the status before and after lumbar sympathectomy so far as night pain, walking ability, and ulceration are concerned.

After attempting to classify these cases in many different categories which might be useful, it became evident that a practical, useful, and simplified classification of four groups was of distinct advantage. Such a classification includes (1) the diabetic with ulceration, (2) the nondiabetic with ulceration, (3) the diabetic with claudication, and (4) the nondiabetic with claudication.

The advantage of grouping these cases in this manner is based not only on the fact that these features are simple, objective, and easily discernible but also because in our series there were definite prognostic differences. In our study other features were included for the sake of comparison, but these did not alter the general prognostic significance of each of the four groups.

Prior to the study we felt that the presence of diabetes and the age of the patient would be important in estimating the prognosis, but we shortly found that these factors were not nearly so important as the presence of ulceration or claudication alone (Figs. 1 and 2).

Ulceration or early gangrene was present in 55 patients, 25 of whom were diabetics and 30 of whom were nondiabetics (Groups 1 and 2 in Table). In these patients the amputation rate was 71%, and 42% had died of associated disease within three years. The age of the patient or the absence of diabetes did not seem to lessen the course of the disease providing ulceration was pres-

Read at the 65th Annual Meeting of the Western Surgical Association, Salt Lake City, Nov. 22, 1957.

From the Department of Surgery, Veterans' Administration Hospital, Dearborn, Mich.; Wayne State University College of Medicine and the Receiving Hospital of the City of Detroit.

Data on Patients with Peripheral Arterial Insufficiency Treated by Sympathectomy

Group	Preoperative Characteristics						Results of Sympathectomy *						
	No. of Patients	Average Age at Time of Surgery	Ulceration	Claudication	Diabetes	Night Pain	Impotency	Mortality	Amputation	Felt Better	Return to 75% Work	Able to Walk Farther	Night Pain Relieved	Ulcer Healed
1. Diabetic with ulceration	25	60				80%	64%	44%	72%	20%	8%	21%	0%	8%
2. Nondiabetic with ulceration	30	47				89%	22%	40%	70%	33%	17%	17%	6%	13%
Ulceration	55	53			45%	84%	41%	42%	71%	27%	13%	19%	4%	11%
3. Diabetic with claudication	11	58				56%	78%	18%	27%	27%	27%	0%	0%	
4. Nondiabetic with claudication	74	49				79%	54%	18%	14%	34%	27%	20%	25%	
Claudication	85	50			13%	76%	57%	18%	15%	33%	27%	17%	22%	
Diabetics	36	60	69%	31%		70%	70%	36%	58%	22%	14%	13%	0%	
Nondiabetics	104	49	29%	71%		81%	47%	24%	30%	34%	24%	19%	20%	
Total series	140	52	39%	61%	26%	78%	52%	27%	37%	31%	20%	18%	16%	

* Results represent the three-year prognosis in each group.

Fig. 1.—Amputation rate within three years.

ent. These figures may be compared with those when claudication alone was present, in which case the amputation rate was 15% and the mortality was 18% within three years. We interpreted this to mean that when ulceration had occurred, the disease has apparently reached a more advanced stage and appeared to progress in spite of treatment.[11] Eleven per cent of the ulcers, however, did heal with good surgical treatment.

Claudication alone was present in 85 patients (Groups 3 and 4 in Table). These patients were classified according to the distance they could walk prior to lumbar sympathectomy and the greatest distance they could walk at any time after sympathectomy. Of these, 57% could walk less than one block; 21%, one to two blocks, and 22%, two or more blocks before claudication occurred. After surgery there was little change in the percentage of patients who could walk each distance (Fig. 3). As a direct question, each patient was asked whether he felt that sympathectomy was effective in increasing his walking ability. Of all patients, 18% felt they could walk farther; another 18% walked a shorter

Fig. 2.—Mortality rate within three years.

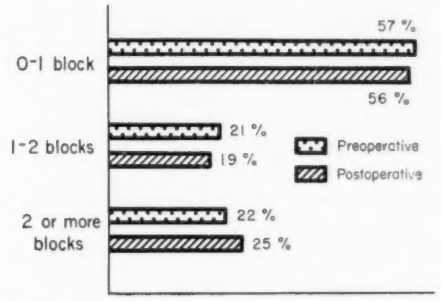

Fig. 3.—Onset of claudication before and after sympathectomy.

distance, and 64% were unimproved (Fig. 4). The greatest improvement occurred in those who, before surgery, could walk more than two blocks. Night pain was present in three-fourths of 102 patients still living. Sixteen per cent of those with night pain were relieved of this pain after sympathectomy.

Possibly our diabetics as a group did less well than nondiabetics, as has been noted by others[2,9]; but the average age of the diabetic was 11 years higher and ulceration occurred in 69% (as compared with 29% of the nondiabetics), and this may well have played an important part. As the figure indicates, however, the diabetic who was treated for claudication alone had little more chance of amputation or death than the nondiabetic with claudication, in spite of the older age. Likewise, the nondiabetic with ulceration did just as poorly as the diabetic with ulceration, who was on an average 13 years older. This indicated to us that it was not the diabetes or age alone but the ulceration that gave the poorer prognosis. One might expect the diabetic with arteriosclerosis to be younger than the nondiabetic, and this may well be true of the patient who has been a diabetic since an early age. Three out of four diabetics, however, are not recognized until after the age of 50,[7] which delay probably accounts for the diabetics in our series being on an average 11 years older than the nondiabetics with symptomatic arterio-occlusive disease. Berry[2] and others have likewise found the diabetic with symptomatic disease to be in an older age group.

The statistical data would indicate that supportive treatment with lumbar sympathectomy has been beneficial in a certain number of patients. Unfortunately, there is no group of similar patients in which sympathectomy was not done for comparison. In our group of patients, 58% of the patients with ulceration were still alive an average of three years after the operation, whereas 82% of those with claudication were still alive. Of those with ulceration, 29% had not had amputation during an average postoperative period of three years, as compared with 85% of those with claudication. In most patients the extremity was warmer objectively and subjectively after the operation, but only 31% of the group felt that the function of the leg had been improved. Of the entire group 20% returned to 75% of full-time employment; 18% of the patients were able to walk farther after sympathectomy; 16% with night pain were relieved, and 11% of patients with ulceration had their ulcers healed.

Comment

The patient with symptomatic peripheral arterial insufficiency has usually had claudication occur after walking less than two blocks, or an arteriosclerotic type of ulceration occurring about the lateral aspect of the lower leg or dorsum of the foot or toes. Atrophy of the skin and muscle, loss of hair, and feeble or absent pulses confirm

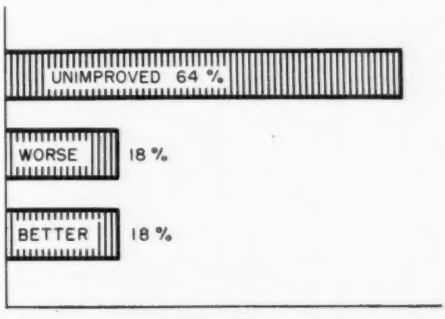

Fig. 4.—Walking ability after sympathectomy.

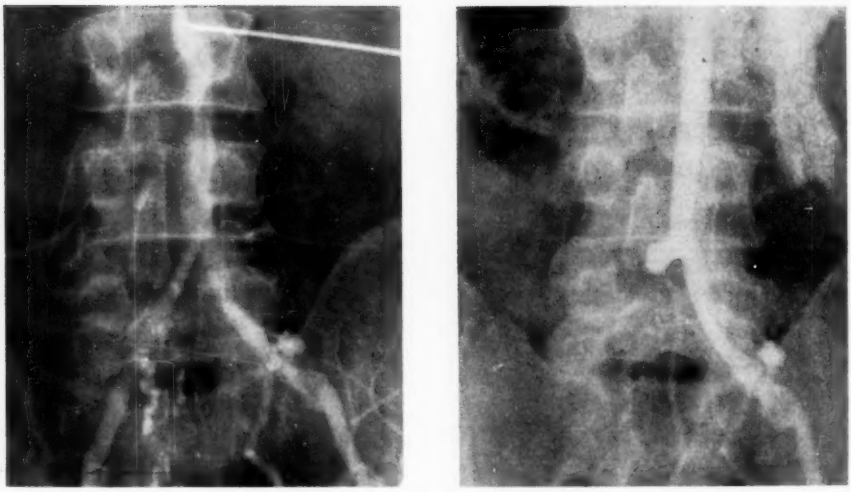

Fig. 5.—Arteriographic changes in a nondiabetic patient over two years.

the diagnosis of arterial insufficiency. The prognosis for such a person can largely be related to the presence of claudication alone or ulceration, as has been indicated. The presence or absence of diabetes does not appear to be important, providing it is adequately treated.

Arteriosclerosis of the peripheral arteries appears to progress steadily and to vary with the patient and the collateral circulation he is able to develop. The arterial disease may progress quite rapidly, as is shown in Figure 5. This illustration demonstrates arteriographic changes which took place in a nondiabetic 36-year-old patient between 1953 and 1955. This patient still has both legs but can walk less than 100 ft. and is not a good candidate for a graft because of lack of adequate distal segment.

Part of our study was completed to determine the extent to which walking ability could be improved by lumbar sympathectomy and conservative surgical treatment. Although the extremity, after nearly every lumbar sympathectomy, appeared to be warmer, the walking ability was not much improved (Figs. 3 and 4). On the other hand, experience with some 90 by-pass arterial grafts, many extending from the common iliac artery to the popliteal artery, has led us to believe that in selected cases a by-pass graft will give much better relief of claudication than sympathectomy.

Currently, we are studying our new patients, as well as following sympathectomy patients, by means of arteriography to determine the presence of a segmental arterial block. Seventy per cent of the symptomatic patients have been considered candidates for a by-pass type of arterial graft, thus producing a large collateral channel for blood to reach the distal extremity.

If properly selected, usually a patient who could walk one block is relieved of claudication, so that he has unlimited walking ability. The arterial graft has been highly successful in 37 of our patients who previously had had sympathectomy. The greatest effect has been in the relief of claudication and improvement of walking ability in our cases, as well as others.[12] It is obvious, of course, that arteriosclerosis is a generalized disease and that it may progress in spite of this treatment.[5] Sympathectomy is considered for its effect through release of spasm and development of collateral circulations.[3,5,10] Currently, we reserve it for the patient who is not a candidate for arterial grafting or who has had a recurrence of symptoms through pro-

gressive arterial obstruction following the grafting.

Summary

In this study we have used a simplified classification of peripheral arterial occlusive disease and discuss ulceration, claudication, age, and diabetes as they may affect prognosis. The course of disease which might be expected with available treatment is indicated by the incidence of amputations and mortality in each group. A study is made of claudication and the extent to which walking ability may be increased by current methods of treatment.

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DISCUSSION

DR. D. EMERICK SZILAGYI, Detroit: I believe this study is a valuable contribution, because it throws further light—and perhaps in some ways new light—on the problem of the relative position of sympathectomy in the management of peripheral occlusive disease.

The experiences that my colleagues and I have had coincide in general with the results related by Dr. Robb, with some minor differences regarding mortality. I fully agree with the conclusions that have been drawn, namely, that in the approach to peripheral vascular disease the primary consideration should be given to angioplastic procedures, and that sympathectomy could best be limited to cases in which these direct procedures are not feasible or in which they have failed.

I believe it would not be out of place, however, to mention that, in spite of their general superiority, the long-range results of direct surgical procedures need to be viewed with some caution. The immediate results in Dr. Robb's report, as in the reports of most authors, are, of course, excellent. He reports normal function in 80% to 90% of the cases. However, if one follows the cases for one to four years, there are important factors that lessen the success rate. We all know that the most important of these factors is the inexorable progress of the basic disease, arteriosclerosis. In addition, some of the arterial substitutes used in the past, particularly homografts, show late degenerative changes.

As better plastic materials come into use, the latter factor may be eliminated; but certainly the problem of the natural progress of arteriosclerosis will be an insurmountable problem for a long time to come. Thus, a distinct, though secondary, place remains for sympathectomy.

On watching the late results of angioplastic procedures, our own interest has been rekindled in thromboendarterectomy. In carefully selected cases, particularly in pure aortoiliac occlusion and in short-segment femoral occlusion, the results of thromboendarterectomy has been quite satisfactory.

DR. LOUIS T. PALUMBO, Des Moines, Iowa: During the past 10 years we have performed 305 lumbar sympathectomies upon 217 patients with peripheral vascular occlusive diseases. Bilateral sympathectomy was performed upon 88 patients.

In this total were 39 diabetic patients, representing 18% of the entire series. Sixty-seven, or 30%,

of these patients had an ulcer of the leg, foot, or toes. In the group of patients with peripheral arteriosclerosis, ulcers were present in 28% of the nondiabetics, whereas ulcers were present in 75% of the diabetics.

In general, 83% of the patients in the entire series experienced improvement. The result was considered good in 60% of the cases, fair in 23%, and poor in 17%.

The over-all results were considered excellent to good in 55% of the diabetics, as compared with 65% of the nondiabetics.

It was apparent from our comparative study that the diabetic patient with peripheral arteriosclerosis fared as well as the nondiabetic patient under similar circumstances, and that the same conservatism can, likewise, be applied in the management of the diabetic patient. A greater number may require major amputations; however, the level of amputation and the wound reparative power may be similar to those of the nondiabetic patient. Of six nondiabetics undergoing amputations, the site was above the knee in 50% and below the knee in 50%. Of 10 diabetics, 40% had the amputation below the knee and 40% above the knee, and 20% had a transmetatarsal amputation.

I believe that sympathectomy should be performed at the time of arteriografting.

Dr. Denton A. Cooley, Houston, Texas: Dr. Robb has made a careful and commendable analysis of these cases of arteriosclerotic occlusive disease. This study is important because it reemphasizes the seriousness of this problem not only from the standpoint of the mortality in these patients but also because it reveals the high incidence of major amputation.

In our cases of occlusive disease, we have attempted to restore pulses by the use of arterial grafts and substitutes or by thromboendarterectomy. During the past five years we have used grafts in more than 900 patients with aortic, iliac, and femoral arterial occlusions. In patients whose pulses are restored peripherally, symptoms usually disappear promptly. However, certain recent studies indicate that the immediate result may be enhanced by sympathectomy.

Dr. Stanley Crawford, who is a member of our department at Baylor, has conducted some interesting studies in plethysmographic recordings. He found that in some patients in whom a successful graft was done and pedal pulses were restored the plethysmographic recordings several days later indicated that digital flow was unchanged, or in some instances actually reduced.

Because of these observations, we have recently been employing a lumbar sympathectomy with most of the operations for occlusive arterial disease. In most cases we now perform a localized removal of the fourth and third lumbar ganglia, and sometimes only the fourth ganglion with adjacent chain is removed. By doing such a localized sympathectomy, we expect to avoid some of the troublesome causalgic symptoms which may plague sympathectomy patients after operation. An immediate improvement in digital flow is evident, and we believe the results are more satisfactory.

Dr. Herbert J. Robb, Detroit: I think everyone is pretty much in agreement as to how these patients should be treated and how they should be handled to get the most immediate and the longest possible relief.

We were rather surprised when we discovered such a high three-year amputation and mortality rate in these patients; but considering that it was high only in those who had advanced arterial disease, as evidenced by the ulceration, perhaps this is understandable.

We also were rather surprised that very few patients who had only the sympathectomy and supportive treatment could walk no farther. It was our original impression that they could walk farther, but the study did not bear this out.

It was felt that if the patient was helped considerably by sympathectomy, it should be the treatment of choice. It is a lesser procedure, and if the results were just as good, the less radical procedure is probably best. It is obvious, however, that in the selected case the arterial graft gives much more immediate relief. We feel that, even though arterial occlusion may proceed in other arteries, and deaths may occur from occlusive disease in three to four years, the immediate relief which follows the graft justifies the procedure.

Surgical Parotitis

R. K. GILCHRIST, M.D., and J. R. McANDREW, M.D., Chicago

Surgical parotitis is an acute inflammation of the parotid gland, either unilateral or bilateral, occurring most frequently after surgical procedures. Although it is an infrequent and unexpected complication, it is quite alarming when it does occur. In the past it has carried a high mortality rate and has been regarded in the literature as a grave prognostic sign.

It has long been known that patients developing parotitis [1] were usually seriously ill, in poor general condition, dehydrated, undernourished, and with poor oral hygiene. A dry mouth and a decreased salivary secretion seems to be the principal precursor to the onset of the disease. The highest incidence has occurred after abdominal or genitourinary tract surgery. In 1927 Rankin and Palmer [2] reported a series of 78 cases, 20 of which followed surgery of the rectum or colon. Gustafson,[3] in 1951, reported 80 cases from the University of Michigan from 1932 to 1951. Of the 51 postsurgical cases in this series, 25, or 50%, had had the abdominal cavity opened.

The infection is almost always caused by the Staphylococcus aureus organism. At the turn of the century experimental laboratory work was divided in theory as to whether the infection was a hematogenous invasion of the gland or an ascending infection from the mouth by way of Stensen's duct. The latter theory is now more generally accepted. Frequently the prolonged trauma of pressure on the gland by the anesthetist has been suggested as contributory to the onset of the infection.

From the Department of Surgery, Presbyterian-St. Luke's Hospital.

Read at the 65th Annual Meeting of the Western Surgical Association, Salt Lake City, Nov. 23, 1957.

The diagnosis is easily made by finding an enlarged, tender gland. The onset is usually four to six days after operation, and by far the majority of the cases appear within the first two weeks following surgery. Occasionally the first symptom is pain in the temporomandibular joint, but more frequently there is localized pain and swelling in the gland. A febrile response occurs within the first 24 hours, with temperatures of 102 to 103 F, along with an acute elevation in the leukocyte count. Mortality rates have always been high, varying from 30% to 60% in most series reported. Despite these high figures, however, parotitis has rarely been considered the primary cause of death; rather, it has been looked upon as indicative of a poor prognosis in those already critically ill.

Early treatment was aimed at stimulating salivary secretion by use of mouth washes, chewing gum, and hard lemon candies, along with warm or cold compresses. Determination of abscess formation by fluctuation is very difficult, because the parotid gland is covered by an extremely dense and unyielding fascia. Incision and drainage, therefore, have often been delayed. The resulting scar of the face and fear of injury to the facial nerve have been other reasons given for the delay of surgery. Blair and Padgett,[4] in 1917, advocated early surgical drainage, and Lilienthal,[5] in 1917, advocated splitting the parotid capsule.

Radium and x-ray therapy for local acute infections, including parotitis, was first reported in 1924 by Hodges,[6] who successfully treated five cases of parotitis. This soon became the treatment of choice, followed by surgical incision and drainage if necessary. With the adjunct of intravenous fluids and antibiotics, a decline in the inci-

dence of postoperative parotitis was seen about 1945.

On our service, within the past two years we have seen seven cases of surgical parotitis. We previously had not seen a case since 1941.

Two of our cases occurred in patients with ulcerative colitis. One patient, a girl of 17, had developed a rectovaginal fistula, Bartholin abscesses, perirectal abscesses, and rectal fistulae. She had been acutely ill with her disease for four months, returning to the hospital after recovering from her multiple abscesses, with poor oral hygiene. An emergency total colectomy, abdominoperineal resection, and ileostomy were performed because of severe and uncontrolled hemorrhage. Right parotitis developed on the third postoperative day. During the postoperative period she bled from her abdominal incision and ileostomy incision, requiring a total of 70 blood transfusions during her three months' convalescence. Every wound was infected.

The other patient with ulcerative colitis was a woman of 54, who had had her disease since 1931. She had had an ileostomy performed more than 15 years before. Multiple internal fistulae developed, requiring several small-bowel resections and a partial colectomy, in stages. She was a severe electrolyte problem and was always seriously ill during her hospitalizations. In 1956 an abdominoperineal resection was performed because of rectal fistulae. Right parotitis developed on the fifth postoperative day.

Two cases occurred in patients with acute diverticulitis of the sigmoid colon. One was a woman aged 63 with diverticulitis of the sigmoid adherent to and obstructing the terminal ileum, as well as the sigmoid. She had a decompressing colostomy performed, and a by-pass anastomosis around the obstructed loops of the ileum was done. Later she had an anterior resection and a small-bowel resection, which was followed by a postoperative wound infection with a colon bacillus. Two months following the resection, her colostomy was closed, and she developed right parotitis on the fourth postoperative day. She had a severe dermatitis about her colostomy, which we were not able to control until after the colostomy was closed.

A 67-year-old man was admitted with generalized peritonitis 48 hours after a free perforation of diverticulitis of the sigmoid colon. He developed right parotitis four days after the pelvis was drained, a transverse colostomy performed, and a decompressing gastrostomy tube inserted. This patient was the only one who recovered from his parotitis with x-ray therapy alone.

Two cases occurred after anterior resections for carcinoma of the sigmoid colon. A man of 64, in good condition otherwise, developed bilateral parotitis on the sixth day following his resection. He had no other infections. A woman aged 54, after an anterior resection for a large carcinoma of the lower sigmoid, developed generalized peritonitis, two small-bowel obstructions, multiple intra-abdominal abscesses, and jaundice. This entire chain of events followed a resistant S. aureus infection in the pelvis. Right parotitis was found on the fourth postoperative day following the initial procedure. She died on the 18th postoperative day of a staphylococcic septicemia.

The seventh case occurred in a 42-year-old woman who had a carcinoma of the cervix treated with radiation and then hysterectomy and oophorectomy, in 1951. She developed severe bladder injury, vesicovaginal fistula, pelvic abscess, and peritonitis. This finally resulted in the construction of an artificial ileocecal bladder in 1952. In 1954 she underwent a left nephrectomy for pyelonephritis and a nonfunctioning left kidney. In 1956 she again developed peritonitis from perforation of the colostomy, presumably due to catheter irrigation two days prior to admission. She was critically ill at this time, entering the hospital with an NPN of 150 mg. per 100 cc. Bilateral parotitis developed on the seventh postoperative day. In 1957 this patient developed a stricture of the right ureter from an adhesive band. This was relieved surgically, and the patient is well at present.

All of these patients but one were acutely ill after extensive intra-abdominal surgery, and all were on antibiotic therapy when the parotitis developed. Four cases in which organisms could be cultured were all positive for antibiotic-resistant S. aureus.

All patients were treated with x-rays as an emergency procedure within the first 12 hours after the onset of symptoms and immediately upon making the diagnosis. The dosage of x-rays was 75 r to the gland tissue daily. One patient responded to x-ray therapy alone within 48 hours.

Within 48 to 72 hours, when it appeared clinically that the swelling and pain were progressing despite x-ray therapy, six of the patients were subjected to decompression in the operating room under local 0.5% procaine anesthesia. A hockey-stick incision was started just anterior to the ear, and extended 1 in. to a point just below the

angle of the mandible and then forward below and parallel to the mandible 1 to 1½ inches farther. The parotid capsule was then split a distance of 1 to 2 in., without incising the gland itself. We were impressed by the marked thickening of the parotid capsule, which measured 2 to 3 mm. in each instance. No pus was obtained by needle aspiration in any case. The wound was loosely packed with iodoform gauze, and warm compresses were applied for two to three days.

Relief from pain was almost immediate in each case, and marked reduction of swelling was noticed within the first three to four hours. Recovery occurred in each case during the next three to four days. There was no evidence of abscess formation in any case. Postoperative scarring was minimal. No x-ray therapy was given after the surgical procedure. One death occurred in this series, and that was on the 18th postoperative day, of resistant Staphylococcus infection and septicemia. The parotitis had subsided in the meantime.

Conclusions

1. Resistant S. aureus infections are becoming a serious problem in hospitals today. When the organisms are present, one can expect to see more parotitis as a postoperative complication.

2. Parotitis occurs after a four- to six-day period of restricted oral intake of fluid. We think oral hygiene should be particularly stressed during this period in patients who are seriously ill from inflammatory conditions following abdominal procedures.

3. As soon as the diagnosis of parotitis is made, x-ray therapy should be started.

4. Surgical incision and splitting of the parotid capsule should be done under procaine anesthesia as soon as it appears that symptoms are progressing despite x-ray therapy.

59 E. Madison St. (Dr. Gilchrist).

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DISCUSSION

DR. J. C. THOMAS ROGERS, Urbana, Ill.: Fortunately, the problem of "surgical mumps" confronts the surgeon infrequently in these days of antibiotics and adequate fluid and electrolyte control. However, when this complication does occur, it presents a critical emergency, as Dr. Gilchrist and Dr. McAndrew have so clearly pointed out.

In commenting on this presentation, I wish to describe briefly the treatment for this type of parotitis which seemed to be very effective in my cases some years ago, and which I continue to use when the occasion demands. I devised it chiefly because I had had equivocal results from experience with radiation treatment alone.

At the first sign of swelling and tenderness indicating parotid involvement, I customarily inspect the oral stoma of Stensen's duct on the affected side. Usually the mucosa for a few millimeters about this tiny orifice is obviously inflamed, but without evidence of discharge.

Usually, about 36 hours from the onset of symptoms, a small droplet of purulent material can be expressed from the opening. That does not necessarily indicate suppuration in the gland itself. Rather, it would appear to indicate edematous obstruction of the glandular end of the duct, thereby causing stasis and subsequent purulent material to form and collect in the stomal end.

At that time intradermal and subcutaneous infiltration of procaine is carried out, much as has been described by Dr. McAndrew. A generous incision is made through the dermis about 1 cm. anterior to the ear and over the entire extent of the gland. By blunt dissection, the wound is deepened to the swollen parotid capsule. The capsule is then exposed for about 1.5 cm. throughout the extent of the incision. Multiple punctures are made through the capsule, thereby releasing serous material. I make punctures rather than an incision in order to lessen the risk of injury to branches of the facial nerve. Several silk sutures are placed through the margins of the wound but are not snugged up or tied at that time. The wound is not packed but is allowed to remain open.

After this procedure, cold compresses of hypertonic magnesium sulfate solution are used until the acute phase has subsided. This is usually a

matter of two to three days, sometimes sooner. The sutures already placed are then tied, closing the wound (this is after the subsidence of the acute process), and three days later the sutures are removed.

By the early release of the intracapsulary edematous fluid and promotion of drainage by use of the hypertonic electrolyte solution, the suppurative stage of septic parotitis is rarely encountered. This point has also been emphasized by Dr. McAndrew. The wounds are cosmetically very acceptable.

When radiation therapy is used in my cases, about 300 mg.-hr. of radium is given. This is in the form of gamma-ray exposure at a 2.5 cm. distance. If the radiation is to be used, it should be administered within the first 12 hours of onset. It should in no way influence the incision treatment, unless there is prompt improvement. I have rarely delayed operative action until that time. Thirty-six hours from onset of symptoms has been the arbitrary limit of delay.

It has always seemed to me that the textbook advice—that of waiting for evidence of fluctuation before carrying out incision and drainage for this condition—often results in disaster to the patient before active therapy can begin. Early incisions through the capsule in most instances prevent progressive toxemia, and local suppuration and sloughing of the gland.

I am sure that many of the older surgeons in years past have been confronted with this trying complication in seriously ill patients. It is well that the younger surgeons become familiar with what is presently a rare, but vexing, surgical complication. The prompt and judicious management of the situation may tip the balance favorably in most cases.

I wish to commend the authors on their fine presentation and on renewing our interest in a serious complication of surgery.

Dr. William Bruck, Gallipolis, Ohio: In Cincinnati we see approximately one of these cases every six months, and to my knowledge we have not had to resort to incision and drainage. The patients are treated as soon as the diagnosis is made, and with very large doses of aqueous penicillin, 400,000 units every four hours, or higher if this dose does not seem to be adequate. In addition to this, they are given 15 drops of potassium iodide three or four times a day.

There has been some work to indicate that iodide is concentrated in the parotid gland. To my knowledge, there have been no deaths from this disease during the three years that I have been there, and the patients have universally recovered from surgical parotitis.

(Inquiry since these remarks makes necessary the correction that we feel strong iodine solution U. S. P. to be more efficacious than the penicillin—and strong iodine solution U. S. P. in large doses, 160 to 200 minims [9.9 to 12.4 cc.] per day per os. It may also be given intravenously. The strong iodine solution U. S. P. is believed to act by causing bacteriostasis, due to its antiseptic properties, and by stimulating salivary secretion. [Altemeier, W. A.: Acute Secondary Parotitis, *Surgery* 20:191-199, 1946].)

Dr. Everett P. Coleman, Canton, Ill.: In the 1920's we used to see this condition not infrequently. It was not a common complication, but we saw it from time to time. It was always a very distressing thing, and in my hands the mortality was high. It occurred most commonly after gastric surgery.

In those days, before the time of the Levin tube, we did not let the gastric patient have anything by mouth for one week. Of course, dehydration developed. We hydrated the patient as best we knew how, which was none too good. As he became dehydrated, his mouth became dry. Obviously, the saliva running down the duct is a downhill stream, and bacteria can't travel upward too readily. When that stream stops, the bacteria can ascend and get into the parotid gland. I believe that is the mechanism of the infection developing.

We used to see these cases, and we used to open the glands, early and late. A number of the patients died. Some of them died with bronchopneumonia, too, and it was a very serious complication.

Dr. C. U. Collins, of Peoria, a former member of this Association, who died a few years ago, devised a method of prevention. He used the method that has been referred to by Dr. McAndrew, having the patient put something in his mouth to stimulate the flow of saliva. Following this suggestion, we would give some fluids, as we did in those days, usually under the skin, rather than in the vein, because of febrile reaction from the intravenous solutions. We would then use lemon drops. Dr. Collins used lemon drops, a combination of sweet and sour, not just chewing gum but the really sour lemon drops. This does stimulate saliva. If the patient has enough water in his system, he will develop enough saliva to flow downhill and prevent the ascending infection.

Of course, you don't do that so much after the disease has occurred, after the complication has arisen; but if you get one patient who dies, you will think about it. If there is an awareness of this, and if the patient is given something by mouth, just enough to stimulate saliva, I think the complication will be less frequent. We started this in the 1930's, and I have seen only one case since then. We used to have them not uncommonly.

DR. JAMES BARRETT BROWN, St. Louis: Parotitis is rarely a primary disease but is a symptom of debilitation. With the present-day methods of postoperative care, opening the gland has become a very rare necessity, but if it does need opening, I agree that there is no use waiting for fluctuation.

Good general care of the patient usually suffices, and the parotitis occurs most frequently in debilitating dyscrasias or in nutritional problems. When we operate in this area at all, we come over the tragus and down around the lobe and out onto the face, but in severe infections it is advisable to stay away from cartilage, in order to avoid a chronic chondritis.

In this great age of antibiotics, if there is anyone here who has not heard Mims Gage's famous words, I should like to repeat them. Mims said: "There is no longer any such thing as aseptic surgery. It is penicillin here and penicillin there. Just keep on giving penicillin. It's gotten so I am afraid to stoop over in my own hospital."

Embryology of Congenital Diaphragmatic Hernia

I. Esophageal Hiatus Hernia

WILLIAM P. KLEITSCH, M.D., Omaha

Much has been written on the subject of esophageal hiatus hernia without actually deriving a satisfactory explanation of what the lesions really are or why they should occur. A congenital basis for these hernias is generally accepted as playing an important role in their pathogenesis, although a clearly defined embryologic explanation seems to be lacking. It is the purpose of this study to point out the embryonic processes whose variants may be responsible for the formation of such hernias.

Many classifications of hiatus hernia suffer from an unnecessary complexity. Considering all hernias through the diaphragm, it is convenient and proper to divide them into traumatic and congenital, with the reservation that the latter group will have some acquired elements in their pathogenesis. This classification is one-sided, since the vast majority of diaphragmatic hernias are basically congenital; and it is of little clinical importance, since the identification of traumatic diaphragmatic hernia is seldom difficult. Of the congenital diaphragmatic hernias, those protruding through the esophageal hiatus form the numerically most important group, and they will be considered first in this study.

Classification

Esophageal hiatus hernias can be classified as three basic types.[7] Each type can be identified by its individual embryologic defect and can be identified clinically, in the child or in the adult, by the demonstration of this anatomic defect. In addition, it must be appreciated that the coexistence of more than one defect is not unlikely, and it probably is this fact which has led to the multiplicity of terms in attempting to classify these hernias. The three basic types of hiatus hernia which can be identified are now discussed.

1. *Sliding Esophageal Hiatus Hernia.*—This type of hernia is identified as one in which the esophagocardiac junction has preternatural mobility and slides (prolapses or is pulled) through the esophageal hiatus and into the posterior mediastinum (Fig. 1). This process occurs retroperitoneally (deep to the gastrodiaphragmatic peritoneal reflec-

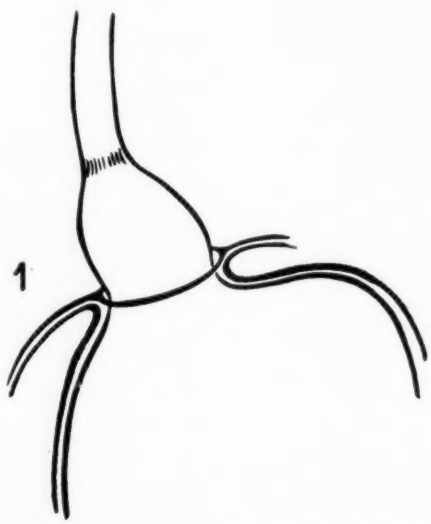

Fig. 1.—Diagram illustrating the sliding type of hiatus hernia. The esophagogastric junction (hatchures) has been displaced upward through the esophageal hiatus. The line below the diaphragm indicates the peritoneal reflection and shows the hernia to be retroperitoneal.

Read at the 65th Annual Meeting of the Western Surgical Association, Salt Lake City, Nov. 23, 1957.

From the Creighton University School of Medicine, the University of Nebraska College of Medicine, and the Veterans' Administration Hospital.

tion), but if the hernia becomes large enough, it can be seen that the peritoneal reflection will be drawn upward into the hiatus (by virtue of the intimate adherence of the gastric serosa to its muscularis), so that an impression of a peritoneal sac may be acquired. This type of hernia (characterized by preternatural mobility of the esophagogastric junction) is so common that it must be considered a normal, anatomic variant. On the other hand, it is also this hernia which is productive of the most violent symptoms. It will be shown that this type of hernia occurs as a result of underdevelopment or maldevelopment of the gastrophrenic ligament.

2. *Paraesophageal Hiatus Hernia.*—This type of esophageal hiatus hernia is one in which the esophagogastric junction remains fixed below the diaphragm by virtue of an intact gastrophrenic ligament. The herniation is into a peritoneum-lined recess, either in front of (ventral to) or behind (dorsal to) the esophagus (Fig. 2). The hernia usually involves stomach or omentum

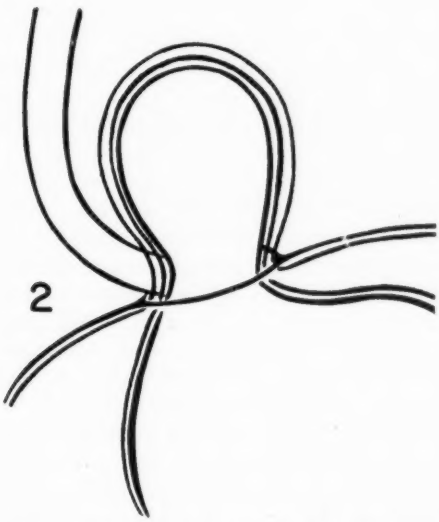

Fig. 2.—Diagram showing the paraesophageal hiatus hernia. The esophagogastric junction is in its normal, subphrenic location, while the fundus of the stomach herniates over it and into a peritoneum-lined recess. The same process may occur behind the esophagus.

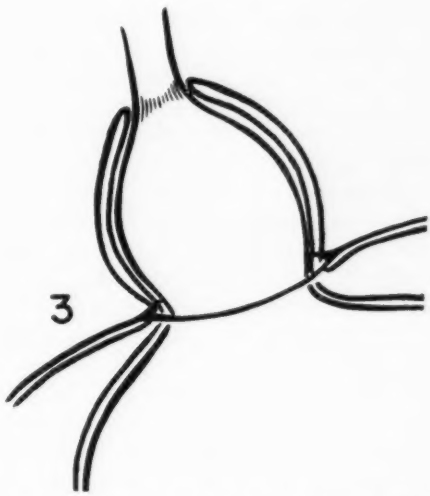

Fig. 3.—Diagram showing the combined form of esophageal hiatus hernia, in which the esophagogastric junction and a large portion of stomach are protruding through the esophageal hiatus and are surrounded by a peritoneum-lined recess.

protruding into the ventral recess. Occasionally, stomach or transverse colon may herniate into the dorsal recess. Probably the most frequent finding is to have the anterior wall of the fundus of the stomach herniated into the ventral recess, over the esophagogastric junction. This situation prompted Allison to describe it as the "rolling type" of hiatus hernia.[1] It will be shown that this hernia is due to the persistence of an embryonic, paraesophageal niche, which presents itself in the adult as a paraesophageal-peritoneal recess.

3. *Combined Esophageal Hiatus Hernia.* This hernia is identified as having the esophagogastric junction above the diaphragm, with a peritoneum-lined recess extending upward to this junction (Fig. 3). This type of esophageal hiatus hernia has been called "congenital short esophagus," although a satisfactory embryologic explanation for such an anomaly is lacking. It will be shown that this type of hiatus hernia is one in which underdevelopment of the gastrophrenic ligament and persistence of the paraesophageal recesses coexist.

Embryology of Sliding Hiatus Hernia

The embryology of sliding hiatus hernia does not involve the diaphragm but is a developmental variant, associated with the embryology of the foregut. In hiatus hernia the diaphragm develops normally. The esophageal hiatus is filled (closed) by structures derived, embryologically, from the mesentery of the foregut, and hiatus hernia is the result of structural variants in the development of this mesentery.

The foregut is that portion of the gastrointestinal tract which extends from the oral plate to the hepatic diverticulum—or from the front of the pharynx to the papilla of Vater. Since this portion of the gut, and the hindgut, is formed by the first bending of the embryo, they are the oldest portions of the gastrointestinal tract and, therefore, are remarkably constant in position.

As the foregut grows, a bulge appears in the center of it which is destined to become the stomach, and from the orad end of the bulge a pouch is formed which grows into the dorsal mesogastrium to become the fundus. In relation to this pouch a mass forms in the left side of the mesogastrium which is to become the spleen, while the dorsal anlage of the pancreas grows into the dorsal mesogastrium between the stomach and the spleen.

As development proceeds, a tremendous overgrowth of the dorsal and left surface of the stomach occurs, and there is a simultaneous growth in size of the pancreas and spleen. These factors, together with the enormous growth of the liver, are partly responsible for the rotation of the stomach on its long axis at the cardia, so that the spleen and the tail of the pancreas come to occupy a position in the left subphrenic fossa.[8] It should be evident that in this process the orad portion of the abdominal dorsal mesentery becomes reduplicated upon itself where it meets the thoracic portion of the dorsal mesentery of the foregut (which is the mesentery of the esophagus), since the esophagus does not rotate as the stomach does (Fig. 4).

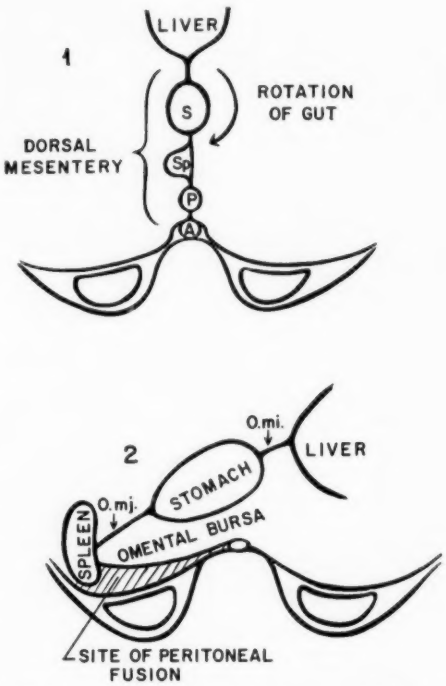

Fig. 4.—Diagram showing how the rotation of the gut and the fusion of the reduplicated dorsal mesentery, above the spleen, forms the splenophrenic, gastrosplenic, and gastrophrenic ligaments.

Not only is this mesentery reduplicated upon itself, it is also subjected to localized, increased, intra-abdominal pressure by the growth of the kidneys and adrenal glands, supplemented by the downward and inward pressure of the muscular diaphragm, which is being forced away from the dorsal body wall by the expanding pleural cavities. Since the fundus of the stomach, spleen, and pancreas are immobile organs, the combination of localized pressure and immobility produces the conditions required for a fusion of the mesenteric layers.[3] Consequently, these layers fuse together and to the dorsal body wall. In this manner the splenocolic, splenophrenic, gastrosplenic, and gastrophrenic ligaments are formed. These are strong ligaments of dense, white connective tissue and serve to anchor the stomach and spleen in the left subphrenic fossa. Imperfections in the development of

these ligaments result in variations in the mobility of these organs.

The gastrophrenic ligament fuses with the ligamentous portion of the left crus of the diaphragm and the median arcuate ligament. It is this ligament which is largely responsible for the orad fixation of the stomach and the subphrenic fixation of the esophagus. Incomplete development of it results in varying degrees of mobility of the gastric cardia. Developmental variations of the length and fixation of this ligament are directly responsible for the occurrence of sliding esophagealhiatus hernias, and reconstruction of this ligament will cure this type of hernia.

It is interesting to note that in this aspect of ontogency the development of the gastric fundus and the cecum have much in common. Both originate as outpouchings of the gastrointestinal tract; both are influenced by the rotation of the gut, and both are fixed to the body wall by secondary mesenteric fusions. It is to be expected that in both there would be considerable variability as to the extent and density of the fusion and, consequently, considerable variability in the mobility of these two organs.

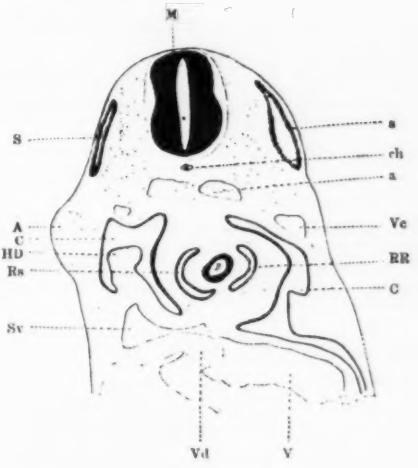

Fig. 6. $\frac{50}{1}$.

Querschnitt eines 3 mm langen menschlichen Embryo in der Höhe der Magenanlage (*D*). Nach Broman (1895).

***a* Aortae descendentes; *A* rechte Armanlage; *ch* Chorda dorsalis; *C* Cölom; *Hd* rechter Leberlappen; *s* Hautmuskelplatte; *Sv* Sinus venosus; *V* Herzvorhof; *Vd* Valvula decrescens; *Rs* „Recessus superior sacci omenti" (= Recessus pneumato-entericus dexter); *RR* der „Ravnsche Rezess" (= Recessus pneumato-entericus sinister).**

Fig. 5.—Reproduction of an illustration from article by I. Broman (*Ergebn. Anat. u. Entwicklngsgesch.* 15:332-409, 1905), showing the two pneumatoenteric recesses in a 3 mm. human embryo (*Rs* and *RR*).

Embryology of Paraesophageal Hiatus Hernia

The lung grows out of the ventral surface of the foregut just caudal to the last pharyngeal pouch and soon divides into two buds within the ventral mesentery. There is some opinion that the lung bud is, in fact, a modified pharyngeal pouch.[2] A seldom-emphasized fact is that both the pharyngeal pouches, as well as the lung buds, seem to stimulate the formation of peritoneal recesses within the celomic tract and in relation to the pouches. The niches usually disappear, but the two in the mesentery may persist, and they are responsible for paraesophageal hiatus hernia.

The paraesophageal niches were first described by Ravn, and later by Broman, who called them pneumatoenteric recesses, since they are blind pouches on either side of the foregut, extending into the mediastinum, above, and communicating with the peritoneal celom, below (Fig. 5). Thus, with rotation of the gut and development of the omentum, the right pneumatoenteric recess will be found to lie behind (dorsal to) the esophagus, and the left pneumatoenteric recess will lie in front of (ventral to) the esophagus (Fig. 6). The right pneumatoenteric recess is quite constantly persistent. It forms the superior recess of the omental bursa and the occasional infracardiac bursa. The left recess is usually described as being transient and quickly obliterated in mammals. However, it seems to me that clinical evidence of the presence of a recess ventral to the esophagus in some adult humans indicates that the left pneumatoenteric re-

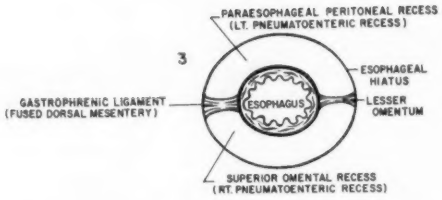

Fig. 6.—Diagram of an adult esophageal hiatus viewed from above and showing the factors involved in hiatus hernia, i. e., the gastrophrenic ligament and the paraesophageal peritoneal recesses.

cess is not as transient as is generally represented.

In this conception, then, paraesophageal hiatus hernia is a hernia into a peritoneal recess and is somewhat comparable to the paraduodenal or paracecal hernias, its greater incidence being explained by the influence of acquired characteristics (obesity, etc.) which affect the basic anatomic variant. It also explains why the esophagus is of normal length in this type of hernia; i. e., the gastrophrenic ligament is intact, permitting the stomach, as Allison points out, to "roll" over the cardiac end of the esophagus and into the ventral (left) paraesophageal (pneumatoenteric) recess.

This also explains how a paraesophageal hiatus hernia may occasionally occur behind the esophagus. In these instances the hernia contents may be stomach, transverse colon, and, rarely, pancreas. In the usual anterior paraesophageal hiatus hernia (into the left pneumatoenteric recess) the organs most frequently involved are anterior wall of stomach, omentum, and, more rarely, transverse colon and spleen.

Embryology of Combined Esophageal Hiatus Hernia

The term "congenital short esophagus" was coined to describe a condition in which most or all of the stomach is found to lie in a peritoneum-lined pouch within the esophageal hiatus and extending into the posterior mediastinum.[6] The esophagogastric junction lies at the apex of the pouch, often as high as the aortic arch, and the esophagus is correspondingly shortened.

First, I shall attempt to refute the validity of the term "congenital short esophagus" on embryologic evidence, or lack of it. Second, I shall attempt to establish the evidence for the term "combined esophageal hiatus hernia."

To begin, one should recall that the foregut runs from the oral plate to the papilla of Vater. These are two, unalterable, fixed points. The pharynx, esophagus, stomach, and duodenum develop out of this fixed length of bowel; obviously, then, one cannot shorten one of these components without lengthening the others. A short esophagus (on a developmental basis) would require a long stomach, duodenum, or pharynx. This is in direct contrast to the descriptions in the reported cases, where the stomach is almost always found to be small and contracted. Furthermore, if the stomach can actually be conceived to have developed above the diaphragm, one must also expect to find its mesentery above the diaphragm, and in the mesentery the spleen and pancreas. In the so-called "congenital short esophagus" the presence of the spleen and pancreas in their proper, subphrenic locations seems to me to be ample proof that the stomach also developed subphrenically and was displaced upward, secondarily, as a hernia.

If one accepts the fact that a congenitally short esophagus has no embryologic explanation, one must yet explain the clinical entity described as such. If one assumes the possibility of the coexistence of the two types of hiatus hernia described above, the embryologic explanation of short esophagus becomes apparent. The anomaly consists of bilateral paraesophageal recesses (persistent penumatoenteric recesses) combined with failure of development of the gastrophrenic ligament. Since the gastrophrenic ligament is not developed, the stomach, instead of rolling over it in the paraesophageal manner, finds itself transported upward in its entirety (as in the sliding type), but the hernia, rather than being retroperitoneal, is into the peritoneum-lined recesses. The

longitudinal muscle of the esophagus accommodates for the shortening, and the bilateral peritoneal recesses form a so-called hernial sac. On an embryologic basis, therefore, it seems appropriate to abandon the term "short esophagus" and substitute for it the term "combined esophageal hiatus hernia." It is probable that this type of defect is present before birth and that the hernia develops in the prenatal period.

Comment

If the above explanation of the anatomic defects in esophageal hiatus hernia is valid, the combined type is the only one which is purely congenital in origin. In both the sliding and the paraesophageal type the basic anatomic defect is seldom in itself sufficient for permanent herniation to develop. With age, however, increased intra-abdominal pressure, possibly the result of heavy labor, obesity, or pregnancy, plays an aggravating role, which can take advantage of the preexisting anatomic defect to produce a permanent hernia. This would explain the greater frequency of hiatus hernias in adult life. Treatment should resolve itself to the surgical correction of the anatomic defect present, rather than to devotion to one technique or another.

The basic surgical principles involved in the repair of esophageal hiatus hernias is to restore the gastrophrenic ligament in the sliding type. In the paraesophageal type the mobile gastric fundus must be fixed, and, secondarily, the paraesophageal recess should be closed by suture. The technique used should be adapted to the individual case.

Combined esophageal hiatus hernia is present from the prenatal period. Anatomic accommodations for the thoracic stomach have been made by the esophagus. They are asymptomatic and require no treatment.

Summary

Esophageal hiatus hernias are classified into three basic types: sliding, paraesophageal, and combined. An embryologic explanation for the anatomic findings in each instance is offered.

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Idiopathic Perforation of the Stomach in the Newborn

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The purpose of this paper is to report three cases of what we propose to call "idiopathic perforation of the stomach in the newborn," and to attempt to crystallize and define this condition as a definite entity by a careful review and analysis of the literature and by splitting off a group of cases which we feel fit our criteria. This task has proved to be a difficult and frustrating one because the literature on this subject includes conditions with many different etiologies.

Siebold, in 1825,[44] reported the first case of perforation of the stomach in the newborn, a case of perforated gastric ulcer in a 2-day-old infant. The first attempt to repair a gastric perforation in the newborn was by Stern,[43] in 1929. Unfortunately, this case was unsuccessful. In 1950 both Leger and his group [23] and Ross, Hill, and Haas [37] reported successful repairs of gastric perforations in the newborn, these infants being the first to survive. In the only successful case of the three we are reporting operation was performed in the same year.

Etiology

In the earlier cases of perforation of the stomach in the newborn reported in the literature, it was thought that all were due to peptic ulcer disease and were so reported. There seems to be no doubt that both gastric and duodenal ulcer may occur in the newborn and that some may perforate, even in the first few days of life. In some cases so reported, however, there is serious doubt in our minds that peptic ulcer disease actually existed, since neither the surgeon nor the pathologist actually demonstrated the ulcer in their reports.[10,12,17,23,35,41-44,46,47,54] It would appear likely, therefore, that some of these cases might well belong in the syndrome which we are trying to define, but we have not included them because of lack of proof.

Other cases of perforation of the stomach in the newborn have been reported as allegedly due to the passage of rubber or polyethylene gastric tubes.[17,20,33,42,49,51,53] Here, again, we concede that such cases may occur but believe the number must be relatively small. Moreover, numerous cases of perforation have occurred without the passage of tubes, and it should be pointed out that in some cases, although a tube was passed, this was done after the onset of symptoms, and in these cases the tube apparently passed through the perforation which already existed. This was true in one of our cases.

A few cases of perforation of the stomach have been reported which were thought to be due to the administration of oxygen under pressure by resuscitator or tube.[30] We have not been greatly impressed with this possibility but feel that we cannot eliminate it as a possible cause in a few cases. In most of the cases we have collected, however, the infants were not given oxygen.

Sepsis is, of course, present in all cases of perforation. In a few cases it is thought that infection antedated the perforation.[17,49] We cannot eliminate this as a possibility but suspect it is rare.

Several other cases of perforated stomach have been reported which were believed to be secondary to intestinal obstruction, including pyloric or duodenal atresia. Anoxia;

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intracranial lesions, such as injuries to the brain and brain tumors [18]; birth trauma,[1,12] and vascular factors, such as thrombosis, embolism, and vascular disease, have all been mentioned in the literature as possible causes.

In 1943 Herbut [15] reported a congenital defect in the muscular layer of the gastric wall of an infant who died of spontaneous perforation of the stomach. He felt that it was the primary condition leading to the perforation and reported microscopic proof of the defect. Since then several others [4,8,25,29,33,37,49] have confirmed this finding. We believe that this is an important contribution to our knowledge of this subject. However, since Herbut's work numerous cases have have been reported in which spontaneous perforation of the stomach has occurred and in which a congenital defect of the gastric wall has not been found, although the clinical picture seemed identical with that in cases reported to have a defect.

After an exacting study of the literature on this subject, and after eliminating all those cases of perforation of the stomach in the newborn thought to be due to peptic ulcer disease, to the passage of a gastric tube, to the administration of oxygen, to trauma of the chest and abdomen, and to obstruction, infection, anoxia, intracranial lesions, and vascular lesions, we still have a group of cases which we feel constitute an entity probably best termed "idiopathic perforation of the stomach in the newborn." For a case to qualify in this category, we recommend that it fulfill the following criteria:

1. The patient must be a newborn infant from a few hours to a few days old.

2. There must be no evidence of peptic ulcer.

3. There must be no evidence of perforation of the stomach by gastric tubes or by the administration of oxygen, nor must there be any significant trauma to the chest or abdomen.

4. There must be no evidence that perforation occurred as the result of obstruction of the intestine, of vascular lesions of the stomach, or of significant cerebral lesions.

Analysis of Cases Which Seem to Fulfill the Criteria

On review of the literature, we have found 40 cases which we feel fit these criteria. A brief review of these cases follows.

Sex.—There were 20 male and 8 female infants, a ratio of 2.5:1.

Age.—The youngest was 11 hours and the oldest 10 days of age at onset of symptoms.

Race.—This apparently plays little or no role.

Syphilis.—Only one case has been reported with a positive Wassermann reaction.

Rh Factor.—Too few cases have been evaluated (three were Rh-positive, and one Rh-negative).

X-Ray Studies.—Twenty-four had x-ray examinations of the abdomen. Of these, 22 showed free air in the peritoneal cavity. Two cases were negative, but at least one of these had no upright films.

Surgical Cases.—Operation was done in 23 cases, with 8 survivals. None of the infants not operated upon survived. One patient survived the initial operation only to have a second perforation, followed by death.

Congenital Defect of Muscular Layer of Stomach.—Thirteen infants were reported to have absence of the muscular layer of the stomach at the site of perforation. In five others [16,28,42] the muscular layers were reported to be thinned out.

Congenital Anomalies.—Six of these infants are reported to have one or more other anomalies. These included a congenital defect of the diaphragm, pyloric atresia, which I did not feel was a factor in the perforation, harelip, cleft palate, Mongoloid features, congenital anomalies of the genitourinary tract, esophageal atresia, diaphragmatic hernia, and hypoplasia of the kidney.

Prematurity.—Nine of these infants were premature, an incidence of prematurity of 22.5%, as compared with a normal of 6%.

Site of Perforation.—Of 30 cases in which it was reported, the site of perforation was at the greater curvature in 22, on the lesser curvature in 4, on the anterior wall in 2, and in the fundus and in the cardia in 1 each.

Clinical Picture

The clinical picture is strikingly uniform and clear-cut and should be easy to diagnose if one has the condition in mind. Typically the infant is born with little or no difficulty, is often small, and frequently premature, with a higher-than-normal incidence of congenital defects. He apparently remains well for a matter of a few hours or a day or two, and it then becomes apparent that he is not doing well. He does not take the feedings well; vomiting may occur, and this is soon followed by abdominal distention, and sometimes with fever. The white blood cell count may be normal, low, or somewhat elevated. On examination, the abdomen is found to be tense, distended, and sometimes edematous. The child is often dyspneic, and even jaundiced.

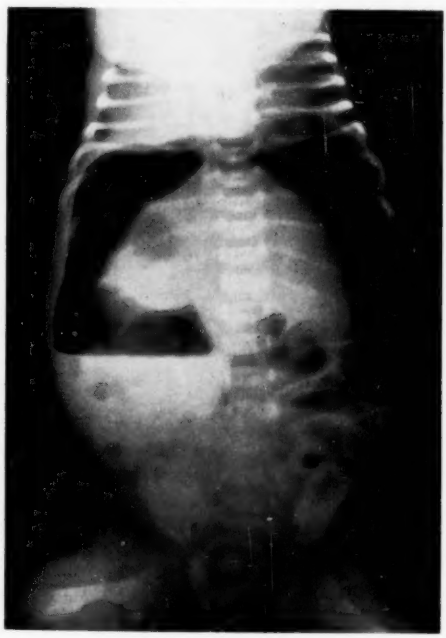
X-ray examination gives a remarkably uniform picture of large amounts of free air in the abdomen, especially in the upper portion. In our three cases the x-ray pictures were nearly identical. The only treatment is surgery, and it must be done early. As soon as the peritoneum is incised, gas escapes under pressure, and evidence of peritonitis is seen. In many cases the site of perforation is plugged with a coagulum of milk. This may be anywhere, but it is commoner along the greater curvature. Simple closure of the perforation is carried out.

Report of Cases

We wish to report three cases of this syndrome, one of them through the courtesy of Dr. Philip M. Howard, of Salt Lake City. There was one survival (Case 1), in 1950, the same year that Léger reported the first survivor from operation for this condition. Case 2 was of especial interest for several reasons. The diagnosis was made preoperatively (probably the first case to be diagnosed preoperatively), because the history and x-ray findings were identical with those in Case 1, which had been seen only 10 or 12 days before. The case was also interesting because the child survived the first operation, only to develop another perforation, which was operated upon with apparent recovery and disappearance of free air, and then a third perforation, from which he died. In all three cases the gastric wall seemed very thin near the site of perforations, although microscopic examination of the tissue was not done.

Case 1.—White boy, born Dec. 9, 1950, and admitted Dec. 11. At 11:15 a. m. on the day of admission it was noted that the abdomen was distended. A picture of shock developed, with rapid respiration, weak pulse, etc. The abdomen was tympanitic and distended. No bowel sounds were heard. X-ray examination showed free air in the peritoneal cavity. The white blood cell count on admission was 3500; the next day it was 12,150.

Fig. 1.—Case 1



An abdominal paracentesis was done to relieve the pressure. A Levin tube was passed to evacuate the stomach. The infant was operated upon Dec. 11. When the abdomen was opened, bile-stained fluid appeared. An opening 1½ in. in length was found in the posterior gastric wall. The Levin tube protruded through the rent. The tissue around the opening seemed very thin, devitalized, and bluish. The perforation was sutured, and the infant made a good recovery and has remained well.

CASE 2.—A white male infant, born Dec. 21, 1950, was admitted Dec. 24, at the age of 3½ days. At 10:00 a. m. on the day of admission, after feeding, grunting respirations developed; the abdomen became markedly distended and tympanitic, and there was absence of bowel sounds. The pulse was 160 a minute; the color poor, and the rectum empty. He vomited several times and had a yellow stool. The white blood cell count was 2000 per cubic millimeter, and the hemoglobin was 22 gm. per 100 cc. An x-ray of the abdomen revealed a large quantity of free peritoneal air, as well as an air-fluid level. Operation was performed on Dec. 24. When the abdomen was opened, bile-stained fluid escaped. A rent 1 in. long was found in the gastric wall on the greater curvature, just anterior to the gastrosplenic ligament. Curds of milk were protruding from the opening, which was repaired with absorbable surgical sutures and black silk. The infant seemed better for four days; then the same symptoms and signs developed, with similar x-ray findings. The infant was again operated upon. The findings were similar, except that there was a new perforation just above the upper end of the suture line. The infant again did well. On Jan. 5, x-ray examination showed no free air, and the abdomen was soft. Later there was a recurrence of symptoms, followed by death on Jan. 18. Autopsy showed reperforation just above the previous perforation. The wall was extremely thin, and there was apparently an absence of muscle layer in the gastric wall.

CASE 3.—A white male infant, was born July 10, 1955, prematurely. Weight at birth was 5 lb. He was admitted on July 14, at the age of 4 days. On the morning of admission the abdomen was noted to be tense and distended, and the infant was bluish, dusky, and lethargic and was vomiting. An x-ray examination of the abdomen showed a large amount of free peritoneal air and fluid. He was operated upon the same day. When the abdomen was opened, bile-stained fluid escaped, together with yellowish-white milk. A large perforation was found on the greater curvature extending almost to the pylorus. The gastric wall appeared thin and deficient. The perforation was closed. The patient died the next day. Autopsy showed the suture line to be intact, and there were no other perforations. There was severe atelectasis in both lungs.

Fig. 2—Case 2

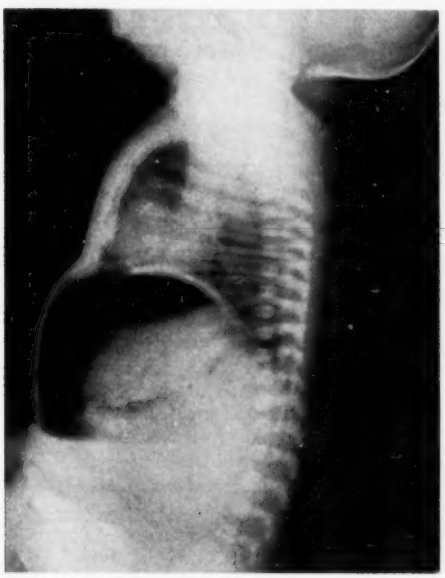
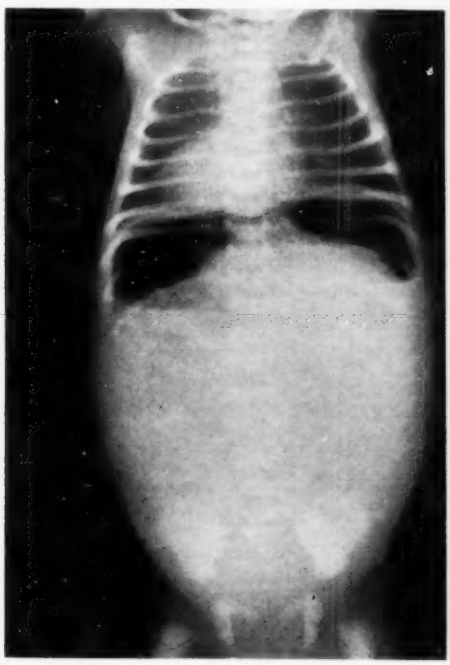


Fig. 3.—Case 3



Comment and Summary

This paper is an attempt to identify what we feel should be recognized as a syndrome, which we will call "idiopathic perforation of the stomach in the newborn." In effect, this group of cases has been split off from a larger group, usually spoken of under the heading of spontaneous perforation of the stomach or rupture of the stomach, etc., by the elimination of cases of perforated stomach in the newborn thought to be due to one of the following: peptic ulcer disease; trauma, especially from the passage of tubes or the administration of oxygen, intracranial lesions; sepsis; anoxia, and any other known cause of perforation, even though we believe it likely that some of the cases reported in the above groups more likely deserve to be in the idiopathic group.

Although the etiology is therefore unknown, it would appear to us that a congenital defect in the musculature of the stomach. It has been reported in a number of cases of this syndrome and perhaps would have been found in others had it been searched for carefully.

The condition is commoner in male infants, is associated with prematurity and congenital anomalies in a higher percentage of cases than would be expected, usually occurs within the first three or four days of life, is easily diagnosed by clinical and x-ray findings if it is kept in mind, and the perforation usually, but not always, occurs at or near the greater curvature. Surgery offers the only hope of cure, and the operation must be done early. Even so, the mortality is high.

We have added 3 cases to the literature, making a total of 43 cases of this type reported.

508 E. South Temple (2).

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DISCUSSION

DR. KENNETH B. CASTLETON, Salt Lake City: I should like to express our appreciation of the opportunity of serving as hosts to the meeting of this Association. For those of you who live in large metropolitan medical centers a meeting of

this type may be a fairly commonplace event, but to us it is a unique experience.

Dr. George B. Packard, Denver: Drs. Castleton and Hatch have so thoroughly covered the subject of gastric perforations in the newborn that my remarks will merely emphasize the need to consider this possibility in an infant who seems to start out in a normal manner, only rather suddenly to show distention of the abdomen and vomiting. The stress mechanism must operate not infrequently in the neonatal period. At the Denver Children's Hospital, we have had, over not too long a period, several cases of gastric bleeding in some of which gastric or duodenal ulcer was shown to be present and which was considered to be of stress origin. Perforation would seem to be much less common in these ulcers.

[Slide] This slide represents the upright film on an infant brought to Denver at the age of 4 days. The mother's labor had been long and difficult, and she had been sick during much of her third trimester. It was reported that the baby had progressed normally for two days, but after that he had been vomiting and his abdomen had been distended. This film, as you see, shows air under the diaphragm. On exploration on the following day, gas and greenish fluid escaped from the abdominal cavity as it was opened. A tiny duodenal perforation was found—it seemed to be sealed, but an omental tag was tacked over it. The baby recovered. He is now 5 years old but is said to show signs of spastic paralysis.

[Slide] The next film, taken with the 5-day-old infant in a supine position, shows the abdomen grossly distended with fluid and gas. The infant had been reported as normal until two days before.

[Slide] The next film, taken in the upright position, shows more strikingly the fluid level and the tremendous amount of free peritoneal gas. Exploration showed general peritonitis with plastic exudate blocking the upper abdominal cavity. The source of the leakage was not found, and prolonged search was not considered advisable. Autopsy revealed a sealed perforated ulcer high on the lesser curvature of the stomach.

These two cases add little to the excellent presentation just heard except to reemphasize that early x-ray diagnosis may allow some salvage in this rare condition. To my knowledge, we have not recognized any case of gastric perforation due to lack of muscle-wall development, to the use of the Levin tube, or to more distal obstruction.

Dr. Eugene A. Osius, Detroit: Those of you who know Dr. C. D. Benson will wonder at the metamorphosis. He is at home tending to the fires. He asked me if I would discuss Dr. Castleton's paper for him. I would like to say, first of all, that I enjoyed this paper very much. Certainly it touched the high points and left a very clear picture in our minds. We appreciate Dr. Castleton's asking us to discuss it.

What I have to report here is entirely Dr. Benson's experience. Although I am also at the Children's Hospital in Detroit, I personally have not had any of these cases; but over the last 12 years we have had 12 of these cases which fit into the category that Dr. Castleton described. In none of them was there any evidence or cause to suspect trauma.

There were a few outstanding features that might be brought out. Six of these infants were female and six were male. This immediately brings a different aspect to the 2.5:1 ratio that Dr. Castleton reported. Ten of the twelve infants weighed less than 6 lb. Seven were premature and five were full-term infants. Of the 12 infants, 5 are living after operation.

The general picture in practically every instance is that the baby is small, weighing 6 lb. or under, and is perfectly well until four or five days after birth, when the following symptomatology begins: usually emesis first, then distention, then dyspnea and occasionally cyanosis, and then the positive evidence of free air in the peritoneal cavity upon examination.

As to the cause, we have no answer. These cases are at the moment being studied a little more fully. We believe the defect of musculature may be a very definite point. On the other hand, an interesting question may be raised: If this is the cause, and if it is the only one, why is it that we do not see more spontaneous perforations after a Ramstedt operation, when we very carefully uncover the mucosa from its surrounding coats and bring it out into the open, so to speak?

In summary, therefore, I may say this: Given a premature infant weighing under 6 lb. who in the first four days of life shows emesis, distention, possible dyspnea, and possibly cyanosis, a perforation should be suspected at once and confirmed with a flat plate and immediate operation performed.

Dr. Charles W. McLaughlin Jr., Omaha: I should like to present the slides in three cases which do not qualify for Dr. Castleton's very beautiful and clear-cut presentation of the spontaneous type of perforation, but which might be confusing to the clinician.

[Slide] This infant was perfectly well at birth and was seen 24 hours later with a marked degree of abdominal distention with tympany. This film shows an amazing amount of air in the free cavity. With a diagnosis of probable perforated ulcer, an exploration was done, and a small perforation was found on the lesser curvature immediately proximal to the pylorus. This was closed, and the infant made an uneventful recovery.

After further interrogation, it was found that on its first day of life this infant had received oxygen by means of an intragastric Polythene catheter. I believe this, therefore, represents an instance of trauma from a Polythene catheter.

[Slide] This was a premature infant weighing just under 4 lb., with a tracheoesophageal fistula which was repaired on the fourth day. A polythene catheter was passed through the site of the anastomosis and carefully positioned in the cardia of the stomach. Obviously, the catheter moved, for on the fourth postoperative day the chest surgeon who had done the repair was distressed when his resident called him and said that the Polythene catheter was emerging through the umbilicus. At this time we saw the infant in consultation. The catheter was emerging through the umbilicus. The abdomen was flat. The infant was very small, and clinically doing very well, with a soft abdomen. Iodized oil, which had been given previously, was readily visible outside the gastric pouch. We elected to treat the child conservatively, and, to our satisfaction, it made a very satisfactory recovery and is now a healthy 12 lb. baby.

[Slide] The third infant was seen in the nursery three hours after birth.

[Slide] This shows a tremendous degree of abdominal distention, which was associated with cyanosis and a respiratory rate of about 4 a minute. After considerable thought, we elected to explore the abdomen through a small incision. We were met by a tremendous gush of fetid, purulent peritoneal fluid, indicative of diffuse peritonitis. The baby improved for about 12 hours and then died rather suddenly.

Autopsy disclosed the presence of a well-established peritonitis, which had obviously developed in utero. There was a perforation in the terminal ileum, thought to be in a Meckel's diverticulum, but the degree of necrosis made absolute microscopic confirmation impossible.

Dr. Floyd F. Hatch, Salt Lake City: First, I wish to thank Dr. Castleton for his courtesy in asking me to collaborate in this work and present these cases. I wish to make a very brief statement and seven points.

1. As a surgical entity this condition is relatively rare. We should have our interns, obstetricians, and pediatricians as conversant with this condition as we are trying to become ourselves.

2. We should have good surgical principles to provide every opportunity for the recovery of these babies by having the people aforementioned aid us in bringing such cases to our attention.

3. There should be prompt medical and pediatric study, and early surgical consultation with decisive action.

4. After surgical cut-down polyethylene tubes should be tied into the saphenous vein near the groin to give adequate blood replacement. Feeding of specific amounts of necessary electrolyte fluids and ascorbic acid should be carried out for several days.

5. Gastric decompression should be done as indicated.

6. Any gastric feeding should be avoided until the peristalsis and the gastrointestinal functions are known to be returning.

7. Surgical repair of the stomach should be done not with one but with several layers, and with an outside layer of nonabsorbable fine (silk) sutures.

Dr. Wayne C. Bartlett, Wichita, Kan.: This slide was sent to me with a patient from out of town. The child was 36 hours old at the time. She had not been fed, and no tubes had been placed in the stomach. The infant was one of a pair of twins delivered by Cesarean section. A few hours after delivery the baby's abdomen became distended. The home physician took a flat x-ray plate and thought the child had an intestinal obstruction. A barium enema was given. I would like to show you the plate.

[Slide] It is rather interesting to note that the man who reported this thought he was dealing with a case of intestinal obstruction at the splenic flexure.

[Slide] There is free air under the diaphragm. The various loops of small bowel may be seen. It is obvious that there is free air in the abdomen, as well as under the diaphragm.

The child was operated upon after a venous section was done. We found a hole in the greater curvature that admitted three fingers. A great deal of free peritoneal fluid and gas was present. The patient died 10 hours postoperatively.

Dr. Kenneth B. Castleton, Salt Lake City: I would like to thank the discussants for their very valuable contributions to this paper.

When Dr. Packard and Dr. McLaughlin showed their slides, I remembered I had not shown you mine. I have three slides, one from each case. They show the large amount of air and the uniformity of these cases, and they are very much like those shown by Dr. Packard and Dr. McLaughlin.

[Slide] This is the first case.

[Slide] This is the lateral view of the second case. This isn't the same case.

[Slide] This is the third case, showing the very large amounts of air.

Results of Surgical Treatment for Severe Chronic Gastritis

EDWARD S. JUDD, M.D., and CHARLES C. EDWARDS, M.D., Rochester, Minn.

When the surgeon has exposed the stomach of a patient suspected of harboring a cancer, peptic ulcer, or some other lesion, with or without a history of hemorrhage, and finds no such lesion, what is the best course for him to pursue? Most surgeons will find themselves in just such a dilemma from time to time. Occasionally it is discovered that the lesion at hand is severe chronic gastritis, which has led the internist, the roentgenologist, and occasionally the endoscopist to make an erroneous diagnosis. Ordinarily, one thinks of gastritis as being entirely a medical problem. When it can be proved that the patient has only chronic gastritis, the surgeon usually avoids surgical intervention, for he has surmised that the results from his efforts will probably be anything but satisfactory. The internist is left with a problem which often proves none too happy from his standpoint, either, and after variable periods of treatment with antacids, bland diets, antispasmodic medications, and liberal amounts of reassurance he still finds his results variable at best. We have had an increasing experience with patients who exhibited severe symptoms, even including repeated hemorrhages, who were given a definite diagnosis of ulcer, polypoid disease, or cancer after thorough study by competent internists, but who were found on surgical exploration to have only severe gastritis. We thought, therefore, that it would be valuable to analyze a series of cases in which this problem had presented itself and to study the long-term results as a possible guide for future management.

Read at the 65th Annual Meeting of the Western Surgical Association, Salt Lake City, Nov. 23, 1957.

Section of Surgery, Mayo Clinic and Mayo Foundation (Dr. Judd). Fellow in Surgery, Mayo Foundation (Dr. Edwards). The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

Background Information

Is surgical treatment justified when nothing more serious than gastritis is present? One of us [1] (E. S. J.) was early impressed with the possibility of serious sequelae of chronic gastritis. The material analyzed in that study was postmortem in nature; in it the stomachs in which proved cancer was present were examined microscopically at some distance from the edge of the gross cancer. It was concluded that in spite of repeated trauma to the specific epithelial elements of the gastric mucosa, namely, the chief and parietal cells, nature made valiant attempts at repair in the form of marked hyperplasia of the mucous cells. It was postulated that, given some unknown stimulus, this extreme overgrowth of mucous epithelium might result in malignant change. Hebbel,[2] in reporting a study of 199 specimens resected from stomachs in which carcinoma was present, concluded that he could find no causal relationship between gastritis and carcinoma. The literature is replete with arguments on both sides of this question, but the stimulus for thought still exists.

Curtis [3] concluded that roentgen examination is actually of little value in establishing the diagnosis of atrophic gastritis. However, roentgenologic studies are of considerable value in establishing the diagnosis of hypertrophic gastritis. Kennedy [4] made the statement that both the roentgenologist and the gastroscopist are unable to differentiate, with any great degree of accuracy,

between gastritis and gastric carcinoma in many cases. He expressed the opinion that there should be no delay in such cases in securing a surgical specimen for biopsy when the patient was found to be suffering from a gastric disease which might pose this differential diagnosis. Gray, Shands, and Thuringer [5] approached the problem in a little different manner, although the basic factors may well have been similar. They studied patients who had had gastrointestinal bleeding without demonstrable cause and had undergone laparotomy. Of these 48 patients, 28 had had no resection, and the other 20 had undergone partial gastrectomy. In the follow-up studies it was found that 63% of those who had not undergone resection experienced further hemorrhage. One of these later submitted to gastric resection, where severe erosive gastritis was found, and the result was satisfactory. Of the group who had undergone resection and on whom follow-up data were available, only two (approximately 11%) had any further bleeding. It was discovered that the results were much better for patients who had had previous hematemesis than for those who had had melena alone. It was also of interest that of the specimens found by the pathologist to be exhibiting extreme changes of gastritis, two came from patients who experienced further bleeding, even after partial gastrectomy.

More recently, Strode [6] argued that it was probably inadvisable at the time of laparotomy to attempt to do more than establish the diagnosis, unless the symptoms were actually severe. However, he left room for gastric resection in the occasional case in which, he admitted, the operation might actually assume the proportions of total gastrectomy. He also alluded to the possibility that severe gastritis might be a precursor of cancer of the stomach. His material was drawn largely from a race group known to be prone to the development not only of gastritis but also of cancer. Strode's discussion centered largely on the "giant" changes in the gastric mucosa known as "Menetrier's disease."

Definition of Terms

We were primarily interested in chronic hypertrophic gastritis, on the one hand, and chronic atrophic gastritis, on the other. In the former the degree of thickening of the gastric mucosa is extremely variable, with marked hypertrophy of the specific epithelial glands and advanced infiltration of lymphocytes. In the atrophic form the mucosa is regularly thinned out, with marked decrease in the rugae and a striking prominence of blood vessels. The absence of chief and parietal cells is uniform, and infiltration with both plasma cells and lymphocytes is rather consistent.

Material and Methods

The records of the Mayo Clinic between Jan. 1, 1946, and Dec. 31, 1950, were examined to obtain the material for this study. To be consistent in selecting the cases, the pathologic diagnosis was employed as the criterion. This enabled us to eliminate immediately alcoholic gastritis or simple acute forms of gastritis, as well as any transitory changes which might confuse the issue. We also were able to eliminate secondary gastritis occurring with some specific anatomic change, such as an obstructing pyloric or duodenal ulcer or coincidental carcinoma of the stomach. We eliminated all cases of gastric polyp, because this would introduce a variable factor. This left us with 51 cases of severe chronic gastritis as the proved surgical pathologic entity without any other coexisting gastric or duodenal disease. All of these patients had been treated surgically, and all had had at least biopsy performed.

Results

Age Range.—The ages of the patients ranged from 33 to 65 years, the average age being 50.2 years.

Clinical Diagnosis.—The preoperative clinical diagnosis proved to be extremely variable and difficult. In a great majority of the cases there was unequivocal x-ray evidence of serious gastric or duodenal disease. It was striking how often the roentgenologist was convinced that a cancer of the stomach was present. In other cases he was not so certain but his wording of his impression was strong enough that the clinician accepted this as a warning that a ma-

lignant tumor might be present. Gastric ulcer was suspected from the roentgenogram in many of the cases, and duodenal ulcer in only a few. In several instances gastric polyps were reported by the roentgenologist, but on subsequent review of the specimen only marked hypertrophy of the mucosa was found. The diagnosis that we considered most seriously was that of the clinician who had access to all of the various aids and diagnostic adjuncts. It was striking to note how often a specific unquestioned diagnosis of tumor or cancer was made. In a few cases gastric hemorrhage was the only diagnosis, but this, of course, left the surgeon with no alternative except surgical treatment.

Gastric Acidity.—Gastric analysis appears to have made only a minor contribution to the diagnosis, as only a few of the records seem to stress that laboratory aid. It would be expected that the incidence of achlorhydria would be extremely high with such a diffuse change present in the mucosa, but data were not sufficient to be statistically significant. Relative achlorhydria appeared common.

Gastroscopy.—Apparently the time covered by our study came after the great wave of enthusiasm for gastroscopy had passed. The gastroscopist apparently had realized his limitations, as these cases are exactly the type in which extensive gastroscopic survey would have been performed in earlier years, but in our series not much emphasis was placed on that examination. The findings recorded by the gastroscopist in those patients examined by him are given in Table 1.

TABLE 1.—*Results of Gastroscopy in Twenty Cases of Proved Gastritis*

Gastroscopist's Impression	No. of Cases
Carcinoma	6
Atrophic gastritis	4
Either gastritis or carcinoma	2
Suspect carcinoma	1
Carcinoma cannot be excluded	1
Possible lymphoblastoma	1
Prepyloric ulcer	1
Hypertrophic gastritis	1
Contracture in middle of stomach	1
Poor visualization	1
Indeterminate	1
Total	20

Type of Operation.—The over-all results of surgical treatment fell into three main categories, according to the surgical procedure that had been carried out. We found that of the 51 patients, 32 had been treated immediately by partial gastrectomy; these will be known as the "resection group." In 17 of these either gastric or duodenal ulcer was the clinical diagnosis. Sixteen other patients had undergone gastrotomy with internal examination of the stomach and biopsy of at least one area of the mucosa; these comprise the "gastrotomy-and-biopsy group." In this category, nine patients were thought to be harboring cancer of the stomach prior to the operation. It was interesting that three other patients after biopsy had submitted to vagotomy; these three will be called the "vagotomy group."

The over-all results of the seven-year follow-up study after surgical management are presented in Table 2. On the whole, the follow-up disclosed relatively satisfactory results, and many of the patients had returned to the clinic repeatedly for check-up roentgenograms and other observations. We had assumed that the results might be most unsatisfactory in view of the diffuse changes present in the gastric mucosa. It came as somewhat of a surprise that the results for two patients could not be classed as anything short of excellent, and it was noted that both had had extensive resections. The large percentage of the resection group found to be enjoying good results was even more of a surprise, as we had feared that any improvement noted at first might have been merely temporary. As one might ex-

TABLE 2.—*Results of Surgical Treatment in Fifty-One Cases of Severe Gastritis*

	Resection	Gastrotomy and Biopsy	Vagotomy
Excellent	2	—	—
Good	21	7	2
Fair	1	2	1
Poor	4	3	—
Lost to follow-up	4	4	—
Total	32	16	3

pect, those patients on whom gastrotomy and biopsy only were performed had a much more variable course after treatment. If the patients with poor results are combined with those "lost to follow-up," it appears that nearly half of the patients were far from satisfied, as the "lost to follow-up" patients may well have sought help elsewhere.

The vagotomy group is much too small for us to draw any conclusions. One would assume that the surgeon, having proved that only gastritis was present, was interested in the least possible surgical intervention and did a vagotomy in the hope that it might be helpful. However, two of the three vagotomized patients were definitely improved. One of these had originally been given a diagnosis of carcinoma of the stomach. This had been made not only by the roentgenologist but also by the gastroscopist at the clinic. The first operation resulted in establishing the correct diagnosis by biopsy. The result following this was extremely poor, so that the patient soon returned to the clinic and insisted on more radical measures. Transabdominal vagotomy was then carried out, and the result following this seems to have improved his condition definitely.

Hemorrhage.—It was of considerable interest to us that only nine of the patients had experienced gastrointestinal hemorrhage before operation, either melena or hematemesis, or both. Those patients who did report hemorrhage had had rather severe difficulty from it. Two of the patients had had only single episodes of bleeding, and both of them reported massive hematemesis. All of the others had had at least two episodes, and most of them had repeated hemorrhages. Almost all of them had had repeated transfusions prior to their admission to the clinic. The analysis according to type of operation is presented in Table 3. We would expect that the larger number of resections appearing in that Table would reflect the surgeon's effort to be more radical in a case of hemorrhage than he might

TABLE 3.—*Hemorrhage After Operation in Cases of Severe Gastritis with History of Hemorrhage Before Operation*

	Number	Bled After Treatment
Resection	6	2
Gastrotomy and biopsy	2	1
Vagotomy	1	—
Total	9	3

have been if that symptom were lacking. Two patients of the resection group continued to bleed after treatment. This comes as no surprise, as we would assume that the gastric remnants would continue to exhibit rather marked alteration from the normal. None of our patients were submitted to total gastrectomy because of hemorrhage alone, however. Just why two of the three patients who had less radical surgical treatment than resection failed to bleed after operation is not clear, as both of them appeared to have had rather marked difficulty prior to surgical treatment. This result is somewhat in keeping with that reported earlier from our institution by Gray, Shands, and Thuringer and seems to us to be a rather significant factor for the surgeon to keep in mind when attempting to make his decision about the proper course to pursue once he has established the correct surgical diagnosis.

Nutritional Problems.—The exact nutritional difficulty experienced by the patient was rather difficult to evaluate from the history prior to operation, and our analysis did nothing to clarify this issue. We were particularly concerned about the nutritional status of patients after surgical treatment (especially gastric resection) and made careful inquiry. Once again it was rather difficult to assess this exactly, but we learned from the prolonged follow-up study that two patients in the resection group had rather severe nutritional problems. They had "dumping syndromes" in the early weeks following resection and have continued to complain of rapid filling, weakness, difficulty in maintaining their weight, and a constant necessity for taking iron and vitamins, and for supportive therapy. A

few patients exhibited the dumping syndrome to some extent in the first month following resection, but the long-term follow-up revealed that this has largely disappeared. In the gastrotomy-and-biopsy group one patient who did not present too severe a problem preoperatively was found to be suffering from severe anemia, which required constant, rather expensive, and elaborate therapy. This patient was far from satisfied with medical management, but the surgeons have not been stimulated to suggest more radical surgical management, either. In general, we found that chronic gastritis of a severe degree presents a great challenge to the medical department.

Postoperative Morbidity.—The complications following surgical management of these patients were in no way remarkable. Comparing the postoperative course with that of the average patient after gastric resection or laparotomy, we found no significant difference. The morbidity was exactly that which accompanies operations of a similar magnitude and in no way was interpreted as being peculiar to the gastritis group. We concluded that the postoperative morbidity alone should not be used as an argument against surgical management.

Mortality Rate.—We were pleased to note that no deaths in the hospital followed surgical treatment for these patients. During the seven-year follow-up period we have learned of the death of only one of the patients. This proved to be due to acute alcoholism and occurred three years after gastric resection for severe gastritis. Postmortem studies failed to disclose any other gastric lesion.

Malignant Degeneration.—None of the patients have yet demonstrated a malignant gastric lesion.

Summary and Conclusions

Severe chronic gastritis (either hypertrophic or atrophic) remains largely a medical problem, although the results with present medical management are not particularly striking. For this study the cases of gastritis in which operation was performed at the Mayo Clinic from 1946 through 1950 were reviewed. In the five-year period we found severe gastritis to be the proved diagnosis in 51 surgical cases. Most of the patients had been operated upon because a more serious lesion was suspected clinically, and that diagnosis was fortified in most instances by x-ray study or gastroscopy or both. Gastritis was proved by biopsy in every instance. Gastric resection was carried out in 32 cases (63%) in the hope that improvement might result. There were no unusual complications and no hospital mortality.

Results from gastric resection were better than we had anticipated. A seven-year follow-up study revealed that 72% of patients who had resections were considerably improved. Mere gastrotomy with biopsy was definitely less successful than resection, although medical management subsequently has kept some of these patients relatively comfortable and vagotomy appears to have helped several.

Nine patients had severe hemorrhages prior to surgical treatment, and three of these continued to bleed even after operation, although two of them had undergone gastric resection.

A malignant lesion of the stomach has not developed in any of these patients as yet.

Thus, when a surgeon is confronted with a problem of severe gastritis, having already committed himself to laparotomy, in the light of present-day morbidity and mortality possibilities, he should consider gastric resection seriously.

Section of Surgery, Mayo Clinic.

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DISCUSSION

DR. GROSVENOR T. ROOT, Oakland, Calif.: I would like to continue the discussion of Dr. Judd's paper along the lines of the relationship of carcinoma to hypertrophic gastritis. I am very glad that Dr. Judd brought this subject before this Association.

The head of our pathology department at Merritt Hospital, Dr. Charles Baker, has always been extremely interested in this matter; in fact, he and Dr. Judd both worked on this problem many years ago, and they have both continued to work on this subject of hypertrophic gastritis and gastritis since that time.

Dr. Baker, in his clinical pathology conferences, frequently shows us a specimen that has been removed surgically. Recently he showed one with a tremendous amount of hypertrophic gastritis, in the center of which was a carcinoma. There were two small ulcers out toward the edge of the hypertrophic area, as it blended into the normal gastric mucosa, which made up the rest of the surgical specimen.

When carcinoma does develop in such a lesion as this, one wonders if it simulates the occasional carcinoma that develops in pseudopolyposis of the colon with chronic ulcerative colitis—not the polyps Dr. Richards talked to us about at the University on Wednesday but the pseudopolyposis in which there is regeneration of the mucosa, in an attempt to heal over the ulcerated areas, and nodular development occurs throughout the large bowel.

On occasions, not only in the gastric cell but in the large-bowel cell of the mucosa, with this terrific stimulus the cells regenerate and hypertrophy and many cells grow and thicken, becoming nodular with cobblestone effect, and once in a while these cells will change from the normal and will show malignant change.

It always amazes me when the liver, which is the greatest regenerating organ in the body, fails to show any malignant change in these areas of regeneration. The nodules in cirrhosis of the liver, and, as you well know, it is these nodules which give it the hobnail effect, are purely regenerating hepatic cells, and we do not see carcinoma develop in these areas, as we do once in a while in an area of hypertrophic gastritis or of pseudopolyposis of the colon.

I am very happy that Dr. Judd has shown us the trouble he has in making this diagnosis, for, as you know, we frequently stumble on this diagnosis when we are operating for a bleeding gastrointestinal lesion, gastric ulcer, or gastric carcinoma.

DR. TOM D. THROCKMORTON, Des Moines, Iowa: I want to ask a question. I can appreciate Dr. Judd's trouble.

We have a young man in our town who owns a gastroscope, too. You don't buy one of these things unless you expect to use it, for it does cost a lot of money. Pretty soon a lot of our patients, whom we had done gastrectomies on, were being gastroscoped, and the diagnosis of marked gastritis was reported after gastrostomy. I asked this young man (he hadn't been at it very long) whether he was sure about the gastritis, and he said he was very sure. I reminded him of a question I had asked one of our members one time. I see him in the back of the room—Dr. Masson. I asked him about the anomalies of the external biliary tract, and he said he had seen quite a few, and they were all in his first 12 cases. [Laughter]

I wonder whether this gastroscopy business isn't about the same. You can use only one eye on this instrument, and so my question to Dr. Judd is this: This young gastroscopist of ours has been at it for quite a while, and he is pretty good, and he still says that when we do a gastrectomy on someone, the patient very often has a widespread gastritis afterward. Apparently, it isn't causing very much trouble, but it is there.

Here we have an operation that may cause gastritis, and, in this particular group, that may cure gastritis. I don't know whether I am coming or going.

DR. EDWARD S. JUDD, Rochester, Minn.: I should like to thank Dr. Root for his comments. I am certainly interested to learn that Dr. Baker is continuing his studies, which we began many years ago.

In regard to Dr. Throckmorton's question: We don't want to tread on anyone's toes concerning gastroscopy, for certainly it is a fine art. If you have ever had it done or seen it done, I am sure you know what I mean. [Laughter]

Postoperative gastritis is a very interesting phenomenon. I think that may well account for some of the changes noted after high gastric resection for duodenal ulcer. We would be delighted to learn, about 10 days after operation, that the free acidity measured in the usual way was zero. However, we would be distressed to find that a year later the patient, although entirely asymptomatic, might then have a certain amount of free acid present. I think the gastritis is a temporary phenomenon, which will clear up in a very short time.

Stenosis of the Sphincter of Oddi as a Cause of Jaundice

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Detroit

Benign stenosis of the sphincter of Oddi is a rare cause of obstructive jaundice in the absence of other abnormalities in the biliary tract. Surgery is required for its recognition and correction.

Stenosis of the sphincter of Oddi is more frequently present in association with biliary tract lithiasis and with either acute or chronic pancreatitis. In these situations, it is sometimes difficult to distinguish precisely stenosis of the sphincter of Oddi from normal variations in the caliber of the duct at the sphincter. The significance of its role in the etiology of obstructive jaundice, biliary tract stones, pancreatitis, and symptoms referable to the biliary tract is also not easily defined. There is good evidence, however, to indicate that stenosis of the sphincter of Oddi is a primary factor in the pathogenesis of these disease states in certain patients.

This report is concerned primarily with patients who were operated upon for obstructive jaundice and in whom stenosis of the sphincter of Oddi was found to be the only cause of the jaundice. Permanent relief of obstructive jaundice after correction of isolated stenosis of the sphincter of Oddi provides the greatest clinical evidence of the importance of this abnormality in the etiology of certain biliary tract disease processes. In this group of patients, induration in the head of the pancreas was frequently observed. Pancreatitis was not recognized clinically before surgery and appeared to be a result of stenosis of the sphincter of Oddi and definitely not the cause of jaundice.

From the Division of General Surgery, Henry Ford Hospital.

Read at the 65th Annual Meeting of the Western Surgical Association, Salt Lake City, Nov. 23, 1957.

Clinical Data

There have been 854 patients in whom exploration of the common bile duct has been carried out from 1935 through 1956 at the Henry Ford Hospital. Throughout this period of time it has been a common practice to pass Bakes dilators through the sphincter of Oddi and to dilate the sphincter whenever the common bile duct is explored. The 3 mm. dilator passes through the normal sphincter. Frequently, the dilator must be massaged through the sphincter, and occasionally this is done with some difficulty.

A precise definition of stenosis of the sphincter of Oddi is difficult. We considered stenosis to be present when it was impossible to pass any probe or dilator through the sphincter, or when the 3 mm. dilator was passed only with great difficulty as the sphincter was dilated. Since in passing the dilator the operator feels the tip of the dilator adjacent to the duodenum, obstruction of the bile duct by a pancreatic lesion, by stricture of the common bile duct, or by any other lesion or abnormality proximal to the sphincter can be identified. Such patients were not included in this study.

In a total of 47 patients, stenosis of the sphincter of Oddi was considered to be present at the time the common bile duct was explored (Tables 1 and 2). Of these, 19 patients were jaundiced at the time of operation, which was carried out to relieve obstructive jaundice (Table 1).

In Table 2 are listed groups of patients who were found to have stenosis of the

TABLE 1.—*Distribution of Patients with Stenosis of Sphincter of Oddi and Jaundice*

Group		Number
I. Isolated stenosis of sphincter with jaundice		6
II. Stenosis of sphincter with jaundice and biliary tract stones		12
A. Stones in gallbladder and common duct	6	
B. Stones in common duct only	5	
C. Stones in gallbladder only	1	
III. Stenosis of sphincter with jaundice and chronic pancreatitis		1
Total no. patients		19

TABLE 2.—*Distribution of Patients with Stenosis of Sphincter of Oddi Without Jaundice*

Group			
I. Never jaundiced			23
A. Stenosis of sphincter with biliary tract stones		9	
1. Stones in gallbladder	3		
2. Stones in common duct	3		
3. Stones in gallbladder and common duct	3		
B. Stenosis of sphincter with biliary tract stones and pancreatitis		8	
C. Stenosis of sphincter with pancreatitis		6	
1. Acute pancreatitis *	1		
2. Chronic relapsing pancreatitis	5		
II. History of jaundice previously			5
A. Isolated stenosis sphincter		1	
B. Stenosis sphincter with biliary tract stones		3	
C. Stenosis sphincter with pancreatitis		1	
Total number patients			28

* Surgery done after pancreatitis subsided.

sphincter of Oddi at the time of surgery but who were not jaundiced; five did give a history of having been jaundiced previously (Category II, Table 2). In two additional patients, stenosis of the sphincter was considered to be present, but the operation was carried out because of recurrent pain thought to be of biliary tract origin; jaundice had never been present, and no other abnormalities were found in the biliary tract or pancreas at the time of surgery.

Jaundice from Isolated Stenosis.—Six patients underwent surgery for obstructive jaundice, only stenosis of the sphincter of Oddi being found as the cause of jaundice. In one additional patient who was not jaundiced at the time of surgery but who gave a history of jaundice on two previous occasions, only stenosis of the sphincter was found at surgery; the gallbladder, pancreas, and bile ducts otherwise were normal.

All of the patients had experienced attacks of right upper abdominal pain. Their ages at the time of surgery ranged from 30 to 73 years. The gallbladder, containing stones, had been removed previously in two patients—6 years previously in one patient and 14 years before in the other patient. No gallbladder remnant or significant cystic duct remained in either patient. The jaundice was moderate in severity.

All of the patients in this group underwent surgery to relieve obstructive jaundice, the usual preoperative diagnosis being common duct stone. In four patients the surgeon observed a mild to moderate degree of induration of the head of the pancreas. In no case was it thought that the pancreatic changes explained the obstruction to flow of bile in the common duct. In all but one of the patients serum amylase determinations had been made preoperatively; the serum amylase levels were all well within normal limits. A biopsy specimen of the head of the pancreas taken in one of the patients was reported as showing normal pancreas microscopically.

The sphincter of Oddi was dilated in three of the patients; transduodenal sphincterotomy was carried out in three. In one of the patients the sphincter appeared hypertrophied and was excised. The gallbladder was removed in two patients. T-tube drainage was instituted in all patients, using the long-arm T-tube in two. The T-tubes were removed after intervals varying up to four months. Cholangiograms made prior to removal of the T-tubes failed to show obstruction in the biliary tract.

Jaundice has not recurred in any of these patients. One patient, in whom sphincterotomy had been performed, did experience an episode of epigastric pain nine months after surgery. He has remained symptom-free during the subsequent two years. The patients have been followed for periods of 2 to 20 years following surgery.

Features of this group of patients may be illustrated by the following case report.

A 55-year-old woman was first seen on March 22, 1937. During the previous year she had experienced attacks of upper abdominal pain. Eight days prior to admission another of these episodes occurred, associated with vomiting, fever, and the gradual appearance of jaundice.

Her physical examination did not disclose any significant abnormalities except for the presence of jaundice. The icteric index was 45. A serum amylase level was 16% of normal. The diagnosis of obstructive jaundice was made.

At operation, the liver, gallbladder, and pancreas were normal in appearance and to palpation. The common bile duct appeared dilated and was opened by the surgeon. No stones were found. When the common duct was irrigated, fluid would not pass into the duodenum. The sphincter of Oddi was found to be markedly stenotic. After considerable difficulty, dilatation of the sphincter was accomplished. A T-tube was left in the common bile duct for four months postoperatively.

This patient is still living and has not had a recurrence of these difficulties.

Stenosis of the Sphincter with Jaundice and Biliary Tract Stones.—In this group, of 12 patients, stenosis of the sphincter of Oddi was found in addition to stones in the biliary tract. The stones varied in number and size. In several patients the stones were very tiny, or only sludge or debris was present, which would be expected to pass through the usual sphincter of Oddi. Of the five patients in whom stones were found to be present only in the common duct, three had previously required cholecystectomy for cholelithiasis.

Induration of the pancreas was observed by the surgeon in five of this group of patients. As in the group of patients with isolated stenosis of the sphincter, pancreatitis was not thought to contribute to the production of jaundice.

In 6 of the 12 patients in this group it was possible to dilate the sphincter with Bakes dilators via the common duct. In one patient a cholecystojejunostomy was also performed. In the remaining six patients the sphincter appeared so stenotic that transduodenal procedures were required—transduodenal sphincterotomy in three and transduodenal dilatation of the sphincter in three. The patients have had no further difficulty with their biliary tract or pancreas since surgery, the follow-up periods varying from 1 to 17 years.

The following case report illustrates features in this group of patients:

A 64-year-old man was seen on March 16, 1955, because of jaundice. A cholecystectomy had been carried out in 1944 for cholelithiasis. His health had been satisfactory otherwise in the past, except for a known duodenal ulcer, which had produced typical symptoms of an active ulcer in 1952 and 1954 and had responded to appropriate therapy.

The present illness started 12 days prior to his admission. Jaundice appeared gradually. He had noticed very little upper abdominal discomfort. At the time of admission, the serum bilirubin was 15.0 mg. per 100 cc.; the serum amylase was 65% of normal. On the basis of these and other studies the diagnosis of obstructive jaundice, possibly of malignant origin, was made and surgery advised.

At operation, the common bile duct was found to be dilated, and only "white bile" was obtained on aspiration. A number of minute stones and debris were removed from the lower end of the duct. The sphincter of Oddi was very tight, and the 3 mm. dilator was passed with considerable difficulty. The sphincter was then dilated up to 7 mm. T-tube drainage was instituted. The head of the pancreas was thought to show a mild to moderate degree of induration.

The jaundice cleared promptly after surgery, and the patient has had no difficulty with the biliary tract subsequently. He did have a period of typical ulcer symptoms in February, 1957, considered to be due to an active duodenal ulcer. These symptoms responded to medical treatment.

Stenosis of the Sphincter and Pancreatitis.—Stenosis of the sphincter of Oddi was found associated with pancreatitis in one jaundiced patients (Table 1); it was observed by the surgeon in one other patient who had been jaundiced previously (Table 2). As shown in Table 2, stenosis was observed more frequently in patients who had never been jaundiced; biliary tract lithiasis was present in eight. Transduodenal sphincterotomy or sphincterectomy was carried out in all but three of these patients. The sphincter was dilated via the common duct in these remaining three patients.

One patient had undergone cholecystectomy for stones previously, at which time exploration of the common bile duct was reported to show no stones. She was first seen in our institution with jaundice and acute pancreatitis, and surgery later revealed only stenosis of the sphincter of Oddi.

Comment

The importance of stenosis of the sphincter of Oddi in association with biliary tract disease has been observed by Trommald and Seabrook,[1] Cole and Grove,[2] Mahorner and Browne,[3] and Cattell and Colcock.[4,5] Doubilet and Mulholland[6] have especially emphasized the importance of this condition in the pathogenesis of chronic pancreatitis. Imamoglu, Perry, and Wangensteen[7] have recently recorded the experimental production of biliary tract stones by constricting the terminal common bile duct. The cases in the series here reported illustrate (1) stenosis of the sphincter as an etiologic factor in obstructive jaundice and pancreatitis, and (2) stenosis of the sphincter associated with biliary tract lithiasis. The relief of obstructive jaundice by correction of isolated stenosis of the sphincter of Oddi demonstrates the reality of this lesion clinically.

Although stenosis of the sphincter of Oddi is established as a pathologic entity, its actual frequency is not established. It is difficult to define precisely the limits of normal for the caliber of the lumen of the sphincter. How frequently stenosis is etiologically related to biliary tract lithiasis is also difficult to determine. It is of great importance that the diagnosis of stenosis of the sphincter of Oddi not become a "wastebasket" type of diagnosis. It should be reserved for sphincters with lumens that are definitely narrow.

Before the diagnosis of stenosis of the sphincter of Oddi is made, the presence of an impacted stone or carcinoma of the ampullary region must be ruled out. Transduodenal investigation or biopsy should be done if the possibility of one of these lesions exists.

Why stenosis of the sphincter of Oddi should at any given time produce obstructive jaundice or an attack of pancreatitis is a matter for conjecture. It is possible that edema may produce greater obstruction in a sphincter already stenotic. In one of the jaundiced patients in whom isolated stenosis was found the sphincter appeared hypertrophied or granulomatous grossly.

In the group of patients demonstrating isolated stenosis of the sphincter as the cause of jaundice, mild to moderate induration of the head of the pancreas was observed frequently by the surgeon. Pancreatitis had not been suspected clinically, was mild if actually present, and was not considered to be a factor in causing the jaundice. Pancreatic changes of a varying degree are certainly to be expected if stenosis of the sphincter is severe enough to produce jaundice. It is also well recognized that it is difficult to distinguish the presence of mild changes in the pancreas by palpation.

Dilatation of the sphincter of Oddi has been carried out as a part of exploration of the common bile duct at the Henry Ford Hospital for many years. In no instance has this procedure been shown to be responsible for stenosis of the sphincter at a later date. The procedure has not been shown to increase the morbidity or mortality for exploration of the common duct.[8] In the patients here reported, whether dilatation of the sphincter via the duct or whether transduodenal sphincterotomy was done depended on the situation present. In general, transduodenal sphincterotomy was performed for severe stenosis or chronic relapsing pancreatitis, or if another lesion in the region of the sphincter was suspected. Whenever dilatation of the sphincter was found to be very difficult, transduodenal sphincterotomy was done. The latter procedure is associated with an increased morbidity and mortality rate.[5]

The results of the surgical procedures in this group of patients were gratifying. In no instance has jaundice recurred, nor has biliary tract surgery again been required.

Summary and Conclusions

Stenosis of the sphincter of Oddi is a rare cause of obstructive jaundice in the absence of other abnormalities of the biliary tract.

Surgical correction of isolated stenosis of the sphincter of Oddi will relieve obstructive jaundice, providing evidence of the clinical importance of this lesion.

A mild to moderate degree of induration in the head of the pancreas frequently is an associated abnormality in obstructive jaundice due to stenosis of the sphincter of Oddi.

Stenosis of the sphincter of Oddi is more frequently present in association with biliary tract lithiasis or pancreatitis in the absence of jaundice.

In our experience dilatation of the sphincter of Oddi is not followed by the production or recurrence of stenosis.

If stenosis of the sphincter of Oddi is pronounced, transduodenal sphincterotomy should be performed.

Before the diagnosis of sphincter of Oddi is made, the presence of an impacted stone or malignancy must be ruled out and the presence of definite narrowing of the lumen of the sphincter demonstrated.

Results of surgical correction of stenosis of the sphincter of Oddi are good.

An evaluation of the sphincter of Oddi should be a routine part of every common-duct exploration.

Henry Ford Hospital. (Dr. Block)

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DISCUSSION

DR. DEWARD O. FERRIS, Rochester, Minn.: Dr. Block and his associates have shown us that stenosis of the sphincter of Oddi may cause jaundice in the absence of other abnormalities of the biliary tract, and also that permanent cure may be obtained by dilatation of the sphincter or by sphincterotomy.

I believe the question uppermost in the minds of most surgeons is just how the diagnosis is to be made. There are four methods available as aids to the detection of obstruction of the lower end of the common bile duct: (1) studies of manometric pressure, (2) cholangiography, (3) operative exploration of the common bile duct, and (4) transduodenal exploration.

I have had little experience with the first method, but I do use operative cholangiography routinely. In the first 185 surgical operations on the biliary tract in which this aid was used, it disclosed stenosis of the sphincter of Oddi as the sole cause of obstruction in only one case, a finding which emphasizes the rarity of the condition. If the patient is not deeply jaundiced, preoperative help may be afforded by the use of intravenous cholangiography, since obstruction of the distal portion of the common duct may be suspected if the opacity of the common duct remains as marked in the 120-minute film as it was in the 60-minute film.

However, since most surgeons are going to rely on exploratory methods of evaluation, a word of caution may be wise. The common bile duct is easily damaged, and extreme care and gentleness are required when it is explored instrumentally. It has become an accepted principle in surgery of the biliary tract that before the common bile duct is closed after choledochotomy the surgeon must demonstrate that there is no obstruction of the distal end of the duct. The passage of a 3 mm. dilator with ease establishes this. In routine exploration of the common bile duct, I feel that no further dilatation should be carried out after patency has been ascertained.

I am sure all of us at times have experienced extreme difficulty in passing a probe, dilator, or scoop through the sphincter of Oddi, even when it is entirely normal. I have used a maneuver borrowed from urology—the use of a filiform bougie to find the normal passage. This is attached to the modified scoop or dilator, which may then be

passed without the danger of producing a false passage. This instrument has been a great help to me in completing satisfactory surgical exploration of the distal common duct.

If the surgeon is not satisfied that the distal end of the common bile duct is normal, the duodenum must be opened to permit inspection, exploration, and possibly biopsy. If stenosis is present, I prefer sphincterotomy.

DR. LESTER R. CHAUNCEY, Portland, Ore.: In our area of the country, in Portland, we are rather interested in this sort of thing, largely because of the influence of Dr. Trommald, who has written a certain amount about it and stirred up a great deal of excitement and interest.

I arise to ask Dr. Block a question. On two different occasions when we operated upon patients who had stenosis of the sphincter but did not have any other pathology—patients who would satisfy the criteria outlined in his third slide—sphincterotomy was carried out but the gallbladder was left in place. The jaundice was relieved, but persistent symptoms necessitated subsequent operations.

One such patient was a doctor's wife, who was very much upset about the second procedure which had to be done. In the second patient a cholecystectomy was done after many months of disabling symptoms, symptoms which promptly cleared up. During the interval between the sphincterotomy and the cholecystectomy, there were indications that perhaps a change in the emptying of the gallbladder was taking place, this being suggested by progressive changes in the oral cholecystogram—possibly an indication of a change in the muscular physiology of the gallbladder, serious enough to necessitate a second operation. We came to believe, from this admittedly small experience, that a cholecystectomy must always accompany a sphincterotomy.

Evidently this is not Dr. Block's conclusion, and I wonder if he would mind discussing this point in his closing remarks.

DR. EARL P. LASHER JR., Seattle: I should like to ask Dr. Block three questions.

First, I have the impression that the first pass at the sphincter is the most successful one. If a second attempt is made, the impression of stenosis may very easily be gained. I wonder if that is Dr. Block's impression also.

Second, did these cases show dilatation of the common duct, and was the stenosis verified at operation by cholangiogram?

Third, I wonder if we could take exception to Dr. Block's choice of terms. He spoke of "sphincterectomy." I doubt whether this is ever accomplished. The sphincter very recently has been restudied by Dr. Boyden, in Seattle, and it is a very extensive and complicated structure.

DR. JOHN T. REYNOLDS, Chicago: I have been interested in the problem of neglected or far-advanced common duct problems, particularly when associated with stricture.

In a patient whose common duct is full of stones and sludge, removal of the stones and proving that the sludge is gone may not be enough. We have seen patients in whom this was done, and yet recurrent symptoms suggested that there was persistent inadequate drainage of the common duct. Presumably, continued crystallization of the bile and/or formation of more stones occurred.

Both Dr. Cole and I have had patients in whom there had developed an extensive fibrosis of the lower end of the common duct. When sphincterotomy was done, stenosis recurred, and it finally became necessary to do an elective reconstruction of the common duct. These are admittedly exceptional instances. Since such occasions do arise, surgeons should be prepared to act accordingly.

It has been our thought that if we find we have to extend the sphincter incision for more than half an inch, and if in that area the common duct looks thick and fibrotic, we anticipate the probability that we will not get a good result. We have deliberately selected such a group of patients as that in which a primary and elective reconstruction of the common duct should be done as the operation of choice.

DR. MELVIN A. BLOCK, Detroit: We certainly appreciate the discussion on this subject.

I am sure that you are aware of the excellent studies and reports that Dr. Ferris has made concerning operative cholangiography and its importance in demonstrating anatomical abnormalities in the biliary tract. It may be difficult to be certain about the status of the lower end of the common bile duct at surgery, and the procedures and maneuvers such as Dr. Ferris described may be of help.

Dr. Chauncey's question introduces the problem of why stenosis of the sphincter of Oddi occurs. We have not carried out studies pertaining to the neuromuscular physiology of this area. Recurrences of stenosis of the sphincter after surgical correction have not occurred in our experience. It is conceivable that recurrence can develop, however.

Why stenosis of the sphincter of Oddi occurs is difficult to ascertain. Whether repeated spasm could ultimately produce stenosis is uncertain. Stenosis, and not spasm, was present at the time of surgery in the patients reported in our series. It is difficult to believe that spasm could persist in severe enough form to produce persistent jaundice. Microscopic studies have been reported indicating the presence of increased fibrosis in sphincters which are stenotic. In one of our patients the sphincter appeared hypertrophic at the time of

surgery, but microscopic studies showed only fibrosis.

I agree that the term "sphincterectomy" may be considered incorrect from the anatomical standpoint. Perhaps "partial sphincterectomy" is not a good term either, but is more correct.

Dr. Lasher asked about criteria for the diagnosis of stenosis of the sphincter of Oddi. As we mentioned, it is difficult to set up definite criteria. We considered stenosis to be present if it was not possible to pass any probe or dilator through the sphincter or if a 3 mm. dilator passed only with great difficulty, with the instrument engaged in the sphincter, as felt through the mobilized duodenum. Larger dilators used subsequently also pass with some difficulty in these patients.

The common bile duct often appeared dilated in these patients at the time of surgery, as reported by the operating surgeon. The degree of dilatation apparently was not very great in many patients, however.

We agree with Dr. Reynolds that it is important to be sure that the sphincter is widely patent at the time exploration of the common bile duct is carried out. This may be helpful in preventing stone formation or permitting a residual stone to pass through the sphincter. Dr. Wangensteen and coworkers have recently reported the experimental production of biliary tract stones by constricting the lower end of the common bile duct. It has been our practice to demonstrate patency and to dilate the sphincter whenever the common bile duct is explored.

Fate of the Patient with Acute Pancreatitis

STEPHEN E. REID, M.D., and JOHN M. DORSEY, M.D., Evanston, Ill.

Confusion exists in the terminology describing the clinical stages of acute pancreatitis and the associated pathology in the pancreas of the patient surviving the initial episode. We believe that this confusion is due to an attempt to label clinically a specific phase of a continuous pathologic process in the pancreas, beginning with edema and progressing to complete fibrosis. That such terminology is misleading is shown by the fact that all of the clinical manifestations of so-called "chronic" pancreatitis—pancreatic insufficiency, cyst formation, and calcification—are found in acute pancreatitis. Furthermore, when the pancreas undergoes complete fibrosis, it becomes an inert structure and should not cause pain. Such patients require only pancreatic supplements.

Terminology should be based on the acute pathology of the pancreas: (1) edema; (2) hemorrhage; (3) necrosis; (4) suppuration, and (5) fat necrosis.

Since our diagnosis must be clinical, the following clinical picture of acute pancreatitis is used:

1. Shock type—confused with acute vascular accidents
2. Peritoneal type—confused with perforated viscus, ulcer, or gallbladder
3. Ileus type—confused with bowel obstruction

The clinical manifestations of acute pancreatitis are (1) pancreatic cysts; (2) biliary tract disease; (3) pancreatic insufficiency; (4) pancreatic calcification, and (5) intractable pain.

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From the Department of Surgery, Evanston Hospital, and Northwestern University Medical School.

We feel, then, that it is the recurrent episode of acute pancreatitis that the surgeon is called upon to treat, and not chronic pancreatitis.

Since a representative amount of pancreatitis has been seen in our hospital, and since the advanced pancreatitic invalid has not been our experience, a follow-up study was made to learn the fate of the patient with acute pancreatitis.

Since 1946 we have observed the course of 100 patients with pancreatic inflammation. There were 52 females and 48 males in this series. The diagnosis in each instance was made by (1) a significant elevation of serum amylase; (2) definite findings at operation; (3) definite evidence at autopsy; (4) pancreatic cysts; (5) pancreatic calcification, or (6) evidence of pancreatic insufficiency.

The serum amylase levels ranged from 250 to 3248 Somogyi units, the upper limit of normal in our laboratory being 150 units. Seventy-two patients were found to have an elevated serum amylase, 24 patients having levels of over 1000 Somogyi units.

In nine patients the diagnosis was made at surgical exploration. In seven patients it was made at autopsy.

Five patients were found to have pancreatic cysts. Three of these cysts were surgically excised, and two patients refused surgery and were definite alcoholics.

Three patients were shown to have pancreatic calcification.

Five patients had evidence of pancreatic insufficiency.

There were 20 hospital deaths. Twelve patients died of acute hemorrhagic pancreatitis. Five patients died of carcinoma of the pancreas, having associated acute pancreatitis. Pancreatitis was considered of

secondary importance in three patients who died. One died of liver disease; one, of kidney disease, and one of urinary extravasation following a transurethral resection.

Eleven patients were lost to our follow-up study. Although most of the total group of patients were from our local area, we were still unable to obtain definite data on these 11 patients. From the data, incomplete as they are, which we have been able to tabulate on these 11 patients, their course seems not to have been contrary to that of patients whose follow-up is complete. Sixty-nine patients were followed for a period of 12 years to 6 months.

Of 100 patients with pancreatitis, 59 were found to have biliary tract pathology. Since a normal gallbladder may fail to visualize during the acute phase of pancreatitis, such x-ray evidence was not considered diagnostic of gallbladder disease. Forty-eight patients were found to have had gallstones either at the time pancreatitis was diagnosed or before. Two patients developed gallstones one and three years after the onset of pancreatitis. Nine patients were found to have chronic cholecystitis without stones.

Only 10 patients with biliary tract pathology had no surgical correction of it. Of these, two patients had elevated blood sugars, one dying as the result of diabetic coma. One patient died of a cerebral vascular accident, and two died of acute hemorrhagic pancreatitis. The remaining five patients have vague abdominal discomfort, not unlike the symptoms of chronic cholecystitis.

Forty-nine patients had biliary tract surgery, and in 32 instances the common bile duct was dilated and explored. Stones were recovered in only eight. In the remaining 24 patients the distal end of the common duct was narrowed. The following procedures were carried out: (1) dilatation, in two patients; (2) sphincterotomy, in two; (3) choledochoduodenostomy, in two, and (4) cholecystojejunostomy, in one. In one other patient the common bile duct was dilated but not explored, and this patient has had no further symptoms.

Four of the patients having common duct explorations developed acute hemorrhagic pancreatitis. Three of these patients died, and one, after a very stormy postoperative course of two months, with a serum amylase level reaching 2083 Somogyi units, recovered and has had no further difficulty in the past five years. Two of these four patients had no previous pancreatitis, and two were operated upon after acute pancreatitis had subsided. One other patient developed acute pancreatitis after a gastric resection for duodenal ulcer.

We have been able to totalize in a parallel period our surgical procedures upon the biliary tract. Since 1946, a total of 1297 cholecystectomies and 75 cholecystostomies have been done. The common bile duct has been explored 237 times, or in about 17% of the cases of biliary tract surgery. Stones were found in 50% of the ducts explored. The incidence, then, of pancreatitis following biliary tract surgery is 0.29%.

We believe, on the basis that 100 patients comprise a statistically significant series, that we are licensed to draw certain conclusions. They at least aid us in our evaluation and treatment of the disease process of which we speak. Obviously, certain of these conclusions are speculative.

Of 100 patients with pancreatitis, 25 had dilated common ducts without stones, of whom 16 were jaundiced and 12 had a stenotic sphincter of Oddi; 9 had acalculous chronic cholecystitis, and 2 had pancreatitis that preceded gallstones.

One may speculate that gallstones had been present and had passed into the duodenum or that the stones had been missed. Another interesting possibility is that biliary tract disease, in this instance, is secondary to pancreatitis, rather than the reverse. Biliary stasis is considered an etiologic factor in gallstone formation.

It is entirely possible that pancreatitis comprises the terminal end of the common bile duct to cause such biliary stasis that biliary tract disease and stones result. We have felt, as does Wangensteen,[1] that a

stenotic sphincter of Oddi adds to this stasis.

If this speculation is tenable, then the dilated biliary tree found in the patient with pancreatitis may not yet have advanced to the stage of gallstone formation.

Conclusions

From this study the following conclusions may be drawn:

1. Acute pancreatitis is the disease process.

2. Pancreatic invalidism that requires extensive surgery for its correction has not been our experience.

3. Progression of acute pancreatitis can be interrupted by (*a*) careful medical management, and (*b*) surgical correction of biliary pathology during the quiescent period.

4. Pancreatitis causes such biliary stasis as to result in (*a*) dilated common bile ducts, (*b*) acalculous cholecystitis, and (*c*) gallstone formation.

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Retrograde Surgical Drainage of Pancreas for Chronic Relapsing Pancreatitis

CHARLES B. PUESTOW, M.D., and WILLIAM J. GILLESBY, M.D., Chicago

The incidence of relapsing pancreatitis following recovery from acute pancreatitis has not clearly been determined. Thompson and Derrick,[29] in a study of 61 cases, found an incidence of recurrence of 64%. Collins and Owens[6] state that most patients who survive acute pancreatitis will not have subsequent attacks. Wilkinson and associates[32] state that between 7% and 15% of patients with acute pancreatitis developed other attacks.

Numerous procedures have been advised for the relief of relapsing pancreatitis, none of them completely satisfactory. We should consider the disease as being primary in some cases and secondary in others.[26] The procedures that will be beneficial in secondary chronic relapsing pancreatitis are, in the main, not satisfactory for the primary type. The secondary type of chronic relapsing pancreatitis is exemplified by those cases in which stones are present in the ampulla of Vater or biliary tract disease is present. Adequate treatment of the biliary tract disease is indicated in these cases.

In the case of primary pancreatitis, we shall discuss the disease as found in the chronic alcoholic patient.[12,20,24] The disease is in the pancreas itself, and operations on the biliary tract or toward the head of the pancreas are unlikely to afford appreciable relief. Lawton and Phillips[17] point to the high incidence of psychosexual maladjustment, occupational inefficiency, and alcoholism in these cases.

Basic Principles

We believe that there are five basic principles which must be understood in arriving at the proper management of this discouraging disease.

1. The pain of chronic relapsing pancreatitis is due to increased intraductal pressure resulting from partial duct obstruction.[7,21]

2. Calcification in the pancreas is due to calcium-soap formation in the pancreatic substance, not calcium formation in the ducts.

3. The obstruction in the pancreatic duct may be in several places. There is an alternate dilatation and stenosis of the ducts.

4. Catarrhal inflammation of the ductal system occurs wherever strictures are present and prevents free communication of fluid from one dilated area to another.

5. We believe that with an adequate drainage of the pancreas there is pancreatic regeneration to some degree, and even a severely "burned-out" pancreas may partially recover.

1. *Pain of Chronic Relapsing Pancreatitis.*—In previous publications we have expressed the belief that perineural inflammation of chronic relapsing pancreatitis is responsible for some of the pain of this disease.[25] We doubt the validity of this stand at present and believe that if the ductal system is adequately decompressed, pain will be relieved.[1,8,30] We have observed

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several patients with external pancreatic fistulae who have had pain similar to that of chronic relapsing pancreatitis when the fistulae became occluded by desiccation of the secretion. Removal of a crust or opening of the fistulous tract relieves the pain within a very short time.[18] Since we have been doing the operation which will be presented later, we have noticed that the pain of chronic relapsing pancreatitis has been relieved.

2. *Calcification in the Pancreas.*—Gross and Comfort [16] have shown that calcification occurs in the substance of the pancreas and it not limited to the pancreatic ducts. We believe that pancreatitis of an acute or a subacute nature with necrosis of some pancreatic tissue first occurs. The necrosis is then replaced by soaps, and later by calcium soaps, which become the calcifications that are seen on x-ray examination in about 50% of these cases. If the necrosis of the pancreas is adjacent to a duct, the calcification will occur in this site and may fall into the duct. We believe it is important to realize that pancreatic calcifications are not calculi in the sense in which gallbladder calculi or renal calculi are so considered. Removal of calcifications that may be found in the duct is not adequate to establish good pancreatic drainage.

3. *"Chain-of-Lakes" Appearance.*—In the type of this disease that is found predominantly in the alcoholic patient, the alternate

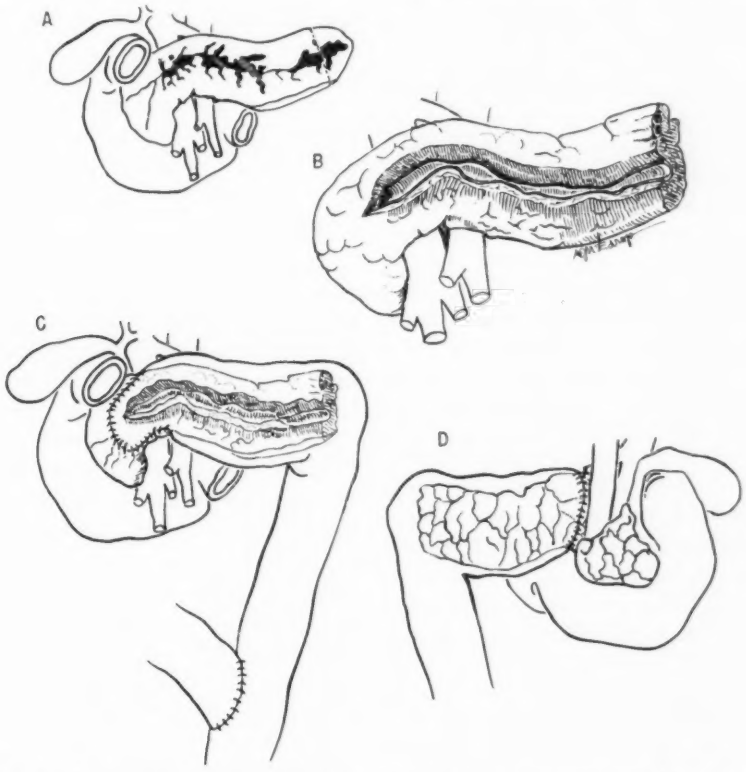

Fig. 1.—*A*, appearance of pancreatic ducts, as seen in some pancreatograms. Note the alternate dilatations and stenoses that are commonly present. *B*, pancreatic duct split open, showing alternate stenotic and dilated areas. Catarrhal inflammation is frequently found at the stenotic narrowing, and calcification may be present at these spots. *C*, anterior view of pancreaticojejunostomy with jejunum sutured to the right of the opened pancreas. Roux-Y enteroanastomosis has been done below the mesocolon. *D*, posterior view of pancreaticojejunostomy with jejunum sutured to the peripancreatic tissue to the left of the superior mesenteric vessels.

dilatations and stenosis of the pancreatic ducts are readily demonstrated by performing pancreatograms either at the operating table or later. In some of these cases we have noticed that there may be as many as seven or eight stenotic areas with areas of dilatation between them. This has been demonstrated at the operating table when the tail of the pancreas has been removed and pancreatic juice spurts from the opened duct under increased pressure. After opening the pancreas along the duct, it has been found that each dilatation has pancreatic juice under similar increased pressure. On x-ray examination it is common to see the duct system as a series of dilatations and stenoses, as shown in Figure 1*A*, which presents a "chain-of-lakes" effect. Warren has made a similar observation.[31]

Noer [22] suggests that ductal dilatation should be demonstrated before retrograde pancreaticojejunostomy. Gray [2] pointed out that scar, fibrosis, and inflammation may prevent ductal dilatation.

4. *Ductal Inflammation.*—We have noted on opening the pancreatic ducts widely that there is an accumulation of mucoid material at the site of each stenosis. This mucoid material is thicker than the usual pancreatic juice and acts as an obstruction to free communication from one dilated area to another. This mucoid secretion has the consistency of white of egg and is stringy and ropy. Solid mucus-plug formation has not been observed. The restriction of free communication of the juice from one dilated area to another has been readily demonstrated at the time of surgery.

5. *Regeneration of the Pancreas.*—Doubilet and Mulholland [10,11] report that the pancreas has the power of regeneration and show by repeated biopsy that there is evidence of pancreatic regeneration. We believe that this contention is valid and that the pancreas can recover to a limited extent even when fibrosed or "burned-out." We base this belief on the observation of a few patients following adequate drainage of the pancreas. One patient had steatorrhea, marked weight loss, foamy stools, and the inability to digest his food in a normal manner.[23] After adequate drainage of the pancreas by the retrograde method, he remained in a state of pancreatic insufficiency for approximately four months. Slowly his stools became normal; his weight began to return to normal, and his digestive situation approached normal. He has been followed for some three years and is in excellent health at the present time, and there is no further evidence of pancreatic insufficiency.

Retrograde Surgical Drainage

The operation of retrograde pancreatic drainage is not a new one. In 1911 Link [18] reported the establishment of an external pancreatic fistula in management of this disease. He mobilized the tail of the pancreas, brought it to the anterior abdominal wall, and established an external pancreatic fistula. The patient was relieved except when the opening closed. Prompt improvement was obtained when the fistula was opened by probing.

In the early 1940's Hunt [5] used retrograde pancreaticojejunostomy in his resections for pancreatic carcinoma. We have been unable to find the reference to this work in the literature, but it is quite possible that his tragic murder occurred before he reported this interesting work. In 1951 Longmire [4,19] performed a caudal pancreaticojejunostomy but abandoned the procedure because it did not appear to help his patient. We began doing caudal pancreatiocjejunostomy early in 1953, and the results were encouraging in the first cases. Zollinger, Keith, and Ellison [33] reported performance of this procedure in 1954, and in the same year DuVal [13] reported his use of this procedure in three cases.

There has been an evolution in the procedure since we first began doing it, and we have now performed the operation in 21 cases. The more recent method will be presented in diagrammatic form.

Present Procedure

Because of the concepts presented above, we believe that caudal pancreaticojejunostomy is an inadequate procedure and that it should be modified as here presented. At laparotomy the gastrocolic omentum is divided and ligated, exposing the body and tail of the pancreas. The spleen is then removed. We have attempted on each occasion to preserve the spleen and have found that it is not practical to do so, owing to the peripancreatitis that exists in these cases. This peripancreatitis makes the separation of the splenic vessels from the pancreas a very difficult procedure, as the perivascular sheath cannot be developed. We have found that it is simpler and safe to remove the spleen. The tail of the pancreas is mobilized as far to the midline as the superior mesenteric vessels. This is generally not a bloody procedure, since the vessels to the tail of the pancreas arise from the splenic vessels and there are a few minor peripancreatic vessels which are easily controlled. The tail of the pancreas is then incised transversely until the duct is found. This exposure of the duct is simple, as we have found that pancreatic juice is ejected under pressure when the duct is encountered. The remaining portion of the amputation of the pancreas is continued and the amputated pancreatic tissue sent for biopsy. A probe is then passed into the pancreatic duct and the pancreatic duct split open as far to the right as is posible (Fig. 1*B*). This brings one to the division of the pancreatic duct into the duct of Santorini and the duct of Wirsung. If the duct of Wirsung or the duct of Santorini is dilated, it is also split open. The bleeding in the edges of the pancreas is controlled by interrupted fine absorbable surgical sutures U. S. P., usually in a mattress fashion. It is not necessary to suture all the way along the opened duct, as the fibrotic pancreas is not a particularly bloody organ. After hemostasis has been secured, one can see pancreatic juice coming from small openings throughout the length of the pancreatic duct. The alternating dilated and stenotic areas of the duct are easily seen, and the rationale for the procedure becomes more apparent. The anastomosis of the pancreas to the jejunum is then accomplished. This is done by dividing the jejunum at a suitable level, generally within a foot of the ligament of Trietz, and bringing the distal segment up through a small opening in the transverse mesocolon. The end of this segment may then be sectioned in a diagonal fashion, so that the anterior portion will fit over the opened duct as far as necessary. We have on most occasions then slipped the tail of the pancreas into the opened, divided jejunum and brought the jejunum to the right, using the jejunum as a sheath over the opened pancreas. The jejunum will come over as far as the superior mesenteric vessels, posteriorly, and as far as the opened duct, anteriorly, if the diagonal severing has been adequate. If not, the antimesenteric border of the jejunum can be split open to permit covering of the opened duct without tension. The edge of the pancreas is then sutured to the edge of the severed jejunum on the anterior surface both superiorly and inferiorly (Fig. 1*C*) and is sutured to the posterior portion of the pancreas to the left of the superior mesenteric vessels by an absorbable surgical suture (Fig. 1*D*). Interrupted cotton sutures are placed in order to accomplish a two-layer anastomosis. The anastomosis is then checked to see that there are no areas where leakage could occur, and the Roux-Y reestablishment of continuity below the mesocolon is then accomplished. The area is drained by means of a split Penrose drain brought out through a stab wound on the left side.[14,15] We feel that drainage is important. We have had two occasions in which pancreatic juice drained for approximately two weeks in small quantities and then ceased.

An alternate method of performing the same procedure is to split the pancreas open as far to the right as practical and then split open the distal portion of the jejunum for

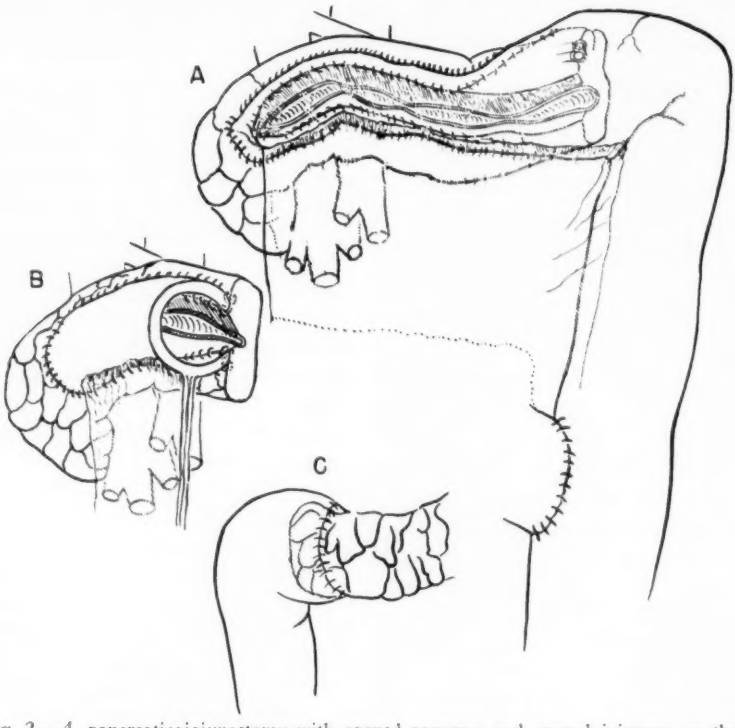

Fig. 2.—*A*, pancreaticojejunostomy with opened pancreas and opened jejunum, so that the pancreaticojejunostomy is a side-to-side anastomosis. Note the anterior position of the jejunal mesentery. *B*, cross section of the pancreaticojejunal anastomosis. *C*, posterior view of the pancreaticojejunal anastomosis.

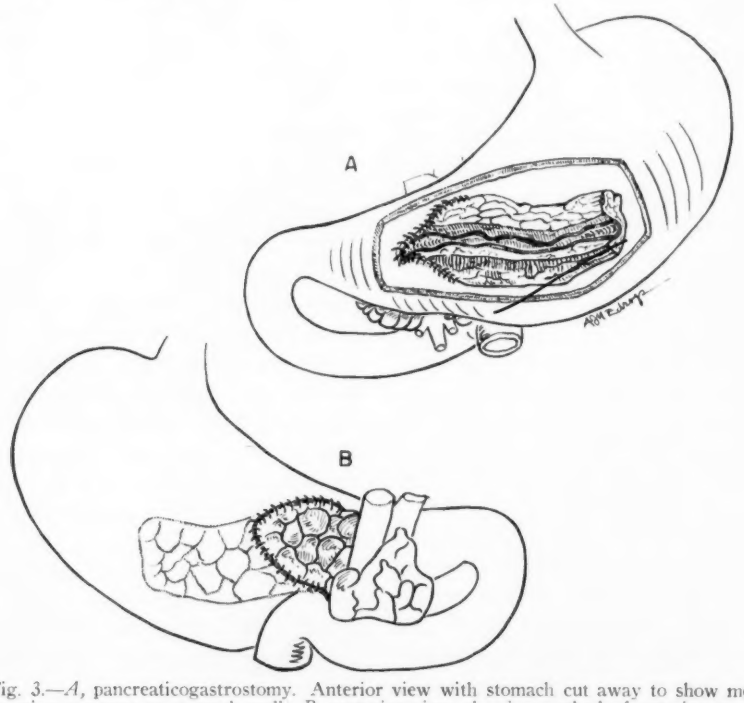

Fig. 3.—*A*, pancreaticogastrostomy. Anterior view with stomach cut away to show method of suturing pancreas to stomach wall. *B*, posterior view, showing method of suturing pancreas to gastrostomy opening.

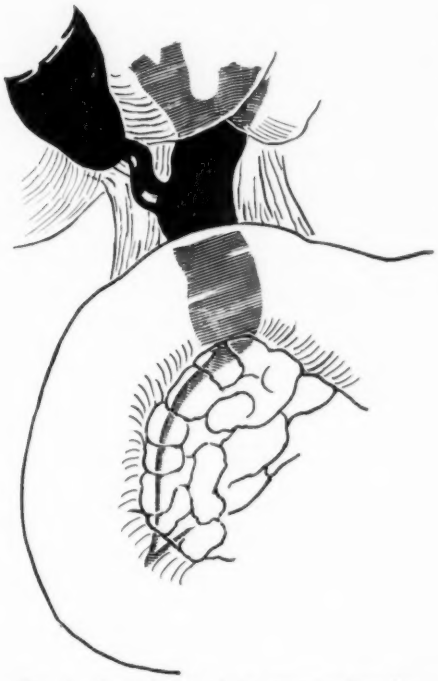

Fig. 4.—Constriction of the common duct due to chronic relapsing pancreatitis, extending from the ampulla for a distance of about 1½ in. toward the liver. Sphincterotomy cannot relieve such an obstruction.

a length of approximately 4 to 6 in. The raw edge of the pancreas is sutured to the raw edge of the jejunum, so that one has, in a sense, a side-to-side anastomosis of the pancreas to the opened jejunum (Fig. 2). We have, in the last two cases, split open the pancreas as far to the right as is technically possible and anastomosed the edges of the pancreas to the edges of the stomach, leaving the opened pancreas in the lumen of the stomach, as in a pancreaticogastrostomy (Fig. 3). The results will be discussed later.

Results

In an analysis of the 21 cases in which pancreaticojejunostomy has been carried out by various methods, we have had no operative mortality. Two patients died later. The first died in a cheap rooming house and, as far as we can determine, was in an alcoholic stupor at the time of his death. The other patient died of an islet-cell carcinoma of the pancreas, approximately two years after the procedure of pancreaticojejunostomy. His case is an interesting one in that we have biopsy tissues taken at three separate occasions: first, when he had a sphincterotomy; second, when he had a pancreaticojejunostomy, and, third, when jaundice developed, due to stricture in the head of the pancreas, as shown in Figure 4, and on all three occasions the biopsies have been reported as "chronic fibrosing or relapsing pancreatitis." We had not seen this patient for some eight months before his last admission, in coma. The blood sugar taken at that time revealed a level of 22 mg. per 100 cc. Dextrose given intravenously revived him, but he continued to have increasingly severe episodes of hypoglycemia and died before any further surgical procedure could be carried out. Autopsy revealed a rapidly growing islet-cell carcinoma of the pancreas with some metastases to the liver—these had not been present at any of the previous surgical procedures. We believe that he developed carcinoma after he had had chronic relapsing pancreatitis. We have no adequate answer as to how to detect carcinoma preoperatively when both conditions are present. Pathologists have pointed out the unreliability of frozen-section biopsy in this situation.[3]

Two patients who were operated upon early in our series have had recurrences of pain, and we believe that they should have reexploration and more adequate drainage of the pancreas or resection of the pancreas, as recommended by Cattell.[5]

Of the last four cases in which the procedure has been performed which we consider adequate—complete opening and exposure of the pancreatic duct and pancreaticojejunostomy, either by the sheath method or by the side-to-side method—the results have been excellent. The recovery time of this procedure, so far as pain is concerned, is almost immediate. So far as nutrition and recovery of the pancreas are

concerned, recovery time may be as high as four to six months. The procedure of pancreaticogastrostomy has been done in two patients. The first patient who had this procedure seemed to be almost normal in about three weeks and has had remarkable recovery, so that now, at the end of eight months, he is back at work and is doing very well. It is of interest that the radiologists have been confused by the presence of the pancreas within the stomach. The second patient who had a pancreaticogastrostomy had rapid recovery following surgery and was in excellent condition for about one month, and then had difficulties of a gastric nature for approximately two weeks. These have disappeared, and he seems to be in good condition; but we are withholding a final opinion as to his status until a later date. The rationale of implanting pancreas within the stomach is subject to doubt. Denson [9] believes that aberrant pancreatic tissue may produce gastric ulceration. Straus [28] has published evidence that a pancreatic cystogastrostomy closes off completely, leaving no communication. This may also occur in pancreaticogastrostomy. Silverstone [27] reports on pancreaticogastrostomy with no adverse effects, but partial gastrectomy may have altered the physiology in his patient.

There has been clinical evidence that regeneration of the pancreas occurs. We have strong clinical evidence in several cases. Time and continued observation will tell us the extent of pancreatic regeneration.

Summary

We believe that chronic relapsing pancreatitis, primary type, is a disease not limited to one portion of the pancreas but exists throughout the pancreatic tissue, and that adequate drainage of the pancreas must be accomplished. In some cases this requires exposing the entire length of the pancreatic duct. We believe that establishment of pancreatic drainage into the intestinal tract is best accomplished by a pancreaticojejunostomy—either by slipping the jejunum over the opened pancreas or by a side-to-side anastomosis. In either case a Roux-Y reconstruction of the gastrointestinal tract is performed.

The procedure of pancreaticogastrostomy has been performed in two cases, but the decision as to whether this procedure is worth while is being withheld at the present time, and we do not recommend it until further observation of these cases.

25 E. Washington St.

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DISCUSSION

ON PAPERS BY DRS. REID AND DORSEY AND DRS. PUESTOW AND GILLESBY.

DR. WILLIS G. DIFFENBAUGH, Chicago: The paper by Dr. Reid and Dr. Dorsey is of great clinical value and very much worth the effort its preparation must have taken.

Raker and Bartlett traced a similar group of cases at the Massachusetts General Hospital and published it in 1953 under the title, "The Fate of the Patient Surviving One or More Acute Attacks of Pancreatitis." Koden and Howard, in 1956, published a paper entitled, "Clinical Studies of the Natural History of Acute Pancreatitis."

Since the inflammatory conditions occurring in the pancreas are progressive, it becomes important to treat the mild attacks, and particularly to correct biliary tract pathology in the quiescent period between attacks.

The other authors mentioned have shown that correction of biliary tract pathology greatly lessens the frequency of subsequent attacks.

I should like to ask Dr. Reid whether he has found a similar result. Whether the biliary tract pathology precipitates the pancreatitis, or the pancreatitis precipitates the biliary tract pathology, has been a controversy for years. In view of Archibald's production of acute pancreatitis by sphincter spasm and Wangensteen's recent production of gallstones by sphincter spasm, is it not a possibility that sphincter spasm or stricture is responsible for both conditions?

The author's experience with acute postoperative hemorrhagic pancreatitis is similar to ours, reported several years ago before this Association. It carries a high mortality.

DR. EDWIN H. ELLISON, Columbus, Ohio: First of all, I should like to congratulate Dr. Puestow and Dr. Gillesby on their very ingenious method for overcoming one of the major objections to retrograde pancreaticojejunostomy, as originally suggested by Dr. Robert Coffey, of Seattle, namely, failure resulting from obstructions proximal to the site of anastomosis. In addition, it embodies the principle of preservation of pancreatic tissue, so often referred to by Dr. Mulholland—certainly an important point to bear in mind if one wishes to avoid subsequent diabetes and the severe malnutrition attendant on pancreatic deficiencies.

Certainly, I have been guilty of removing much-needed and irreplaceable pancreatic tissue in an attempt to minimize the chances of having partial obstructions of the ductal system proximal to the line of pancreatic resection. Furthermore, the procedure would seem to overcome still another objection to the currently employed pancreaticojejunostomy, namely, the possibility of stricture of the anastomosis whenever proximal drainage is

adequate, a condition which, unfortunately, may be intermittent.

One of our associates, Dr. Joseph Bonta, demonstrated this fact several years ago in our laboratory. In this instance, having divided the tail of the pancreas, he implanted both the proximal and the distal end into the small bowel. Almost invariably the isolated tail maintained a patent anastomosis, while the duct of that portion of pancreas which could drain by the normal route closed spontaneously in all animals.

Finally, I should like to borrow some of Dr. Puestow's own statistics. In 1954 the Veterans' Administration Hospitals admitted 1272 cases of acute and chronic pancreatitis. The highest incidence occurred in the most productive decade of life—the fourth decade. This serves to emphasize the importance of adequately controlling the acute phase of pancreatitis in order to lower the increasing incidence of the severely disabling forms of chronic pancreatitis which we have been discussing this morning.

Dr. John T. Reynolds, Chicago: Patients may have pancreatic calcification. We have had one patient with very widespread calcification of the pancreas who, after bilateral splanchnic section, which relieved him of his pain, developed a pancreatic cyst about the size of his head. This was marsupialized. During the following year he periodically discharged calcified material from the pancreas, and the x-ray at the end of a year showed complete cure and softening of all calcification in his pancreas.

An x-ray one and a half years after his cyst was drained showed absence of pancreatic calcification. There were myriads of stones and calcified areas in his pancreas at the time of the original operation.

Dr. Charles B. Puestow, Chicago: The paper given by Drs. Reid and Dorsey was most interesting. About a year ago, when I gave an address on pancreatitis, Dr. Dorsey asked me whether chronic pancreatitis always followed an attack of acute pancreatitis. As I was unable to answer this question, we turned to the literature.

Here we found that in some reports only an occasional patient with pancreatitis gave a history of an initial acute attack. Other authors have reported an initial attack of acute pancreatitis to have existed in as many as 60% of patients with chronic relapsing pancreatitis. With this wide disparity in reports, I do not believe this question is as yet answered. Going back to the literature, I think we should give credit to the man whose name is seldom mentioned. That man is Gage, who was the first to describe the sphincter that is now called the sphincter of Oddi.

Stenosis of the distal end of the common bile duct is often referred to as stenosis of the sphincter of Oddi. I doubt whether stenosis of the sphincter muscle itself is the obstructive factor in many of these cases and whether the partial obstruction usually results from fibrosis of the papilla of Vater or an inadequate opening at its tip.

A year ago I presented before this Association our early work on retrograde pancreaticojejunostomy in the treatment of chronic relapsing pancreatitis. In a number of these operations we placed a polyethylene catheter into the pancreatic duct through its distal end in order subsequently to obtain pancreatograms. All of these have shown a marked stenosis of the pancreatic duct extending from the ampulla of Vater for 2 to 6 cm. toward the tail of the gland. In some patients there was a rather generalized dilatation of the duct distal to the stricture in the head of the gland. In others, there were additional multiple areas of ductal stenosis.

Where the stenosis occurs only in the head of the gland, I do not believe it necessary to lay open the duct throughout the entire length of the tail and body of the gland. However, where multiple strictures occur, it is important to open the duct for a sufficient distance to permit adequate drainage to the head.

Some surgeons recommend resection of the duodenum and the head of the pancreas as far as is needed, to permit good drainage from the remainder of the pancreas. This is an extensive operation, which sacrifices a large amount of an organ which is already diseased and whose physiologic function is markedly impaired. The retrograde pancreaticojejunostomy sacrifices very little of the gland and gives the remaining tissue an opportunity to regain some of its function when pressure upon the secreting cells has been removed.

Our experience leads us to believe that following release of intraductal pressure there may be a marked restoration of pancreatic function. We have had patients in whom the pancreas appeared to be so extensively damaged that we did not believe enough pancreatic tissue remained for adequate physiologic function of this organ. Although some of these patients did not get immediate improvement after operation, there were a gradual return of stools to normal, a gain in weight, relief of pain, and indications of ample pancreatic function.

We have performed many types of nerve resections for the relief of pancreatic pain. Our results in general have been discouraging. It has been most gratifying to us that after retrograde pancreaticojejunostomy the patient's pain is immediately relieved without additional surgery, and that it seldom recurs.

Some reports of this operation have been discouraging. Some surgeons have attempted to make a mucosa-to-mucosa anastomosis between the pan-

creatic duct and the bowel. Such an anstomosis permits only drainage from the main pancreatic duct into the intestine, whereas by implanting the pancreas into the jejunum all divided ducts will drain into it and all pancreatic juice will flow into the intestinal tract. As the loop of jejunum is defunctionalized, there will be little, if any, backflow of intestinal contents to the region of the pancreas.

In summary, with this procedure, we are relieving pancreatic pain, we are minimizing the amount of pancreas that has to be removed, we are restoring to the intestinal tract all pancreatic secretion, and we are performing a procedure which is not difficult and which carries with it very little risk. So far, in our hands it has proved very satisfactory.

Dr. Rudolf J. Noer, Louisville, Ky.: This is an extremely interesting discussion. I would like to add that at least in Louisville pancreatitis is a bad disease. It is not a benign disease at all. The patient who gets pancreatic atrophy, in our experience, gets it only after many severe attacks, with much pain and suffering and much disability. We have had patients go on with pancreatic atrophy even to the point where they have begun to require insulin for atrophy of the islet-cell tissue as well. This, too, is something that should be avoided if at all possible.

I think the work of Drs. Puestow and Gillesby is extremely interesting, and we would do well to follow their advice and operate on these patients earlier.

It would seem that if a patient has three, four, or five attacks of pancreatitis, that should be enough warning to us that we are about to deal with chronic recurrent pancreatitis. It would seem that a logical approach would be, first of all, to see whether there is biliary tract pathology that needs correction. At that time we might attempt, through cholangiography, to find out whether there is by chance a possibility of demonstrating obstruction to the pancreatic duct. I am sure that Dr. Puestow and Dr. Gillesby have demonstrated the utter futility of sphincterotomy when there is pancreatic-duct obstruction. I am sure that the honest enthusiasms for sphincterotomy has set back reasonable treatment of pancreatitis by many years.

In these multiple obstructions along the ductal area, the complete futility of cutting the sphincter beyond the point of obstruction is obvious.

This has been an extremely interesting paper, and I think we would all do well to take a leaf from the book of Drs. Puestow and Gillesby and treat these patients more actively and earlier.

Dr. Stephen E. Reid, Evanston, Ill.: I certainly did not mean to imply that I still believe that chronic pancreatitis invalids do not exist. We do not see them in our hospital.

The question Dr. Diffenbaugh raised concerned what happened to these people who had biliary tract surgery. They have not had any symptoms that we could attribute to pancreatitis. They have vague abdominal complaints. I mentioned those who had no biliary-tract surgery because these symptoms were similar to chronic cholecystitis.

Dr. William J. Gillesby, Chicago: There seems to be an idea among some who have discussed chronic relapsing pancreatitis that if you don't agree with their concepts you are incapable of discussing the subject at all, and that they will defend their beliefs with fists if necessary.

As far as we are concerned, we have presented this procedure. If it is a good procedure, it will endure; if it isn't, all the talk in the world won't make it any better.

As to calcification in the pancreas, the late Dr. Comfort pointed out the difference between calcification in the pancreatic substance and calculi in the duct. In 65 cases of pancreatic pseudocysts at Hines, the diagnosis of calculus in the duct was made in only one. The calculus was removed, and the patient obtained better drainage, but recently I sent a follow-up letter and found that the poor fellow had committed suicide two years after his so-called "cure."

Dr. Tidrick had pointed out that the incidence of suicide in chronic relapsing pancreatitis is approximately 10% to 15%.

We believe this procedure of pancreaticojejunostomy is a physiologic one. We suspect that the procedure of pancreaticogastrostomy is not. At first we thought the pancreaticogastrostomy was a good procedure, but at present we feel somewhat like the small-town idiot. Every small town has one, by the way. He was going down the rode with one end of a rope in his hand and the other end trailing in the dust. Someone asked: "Zeke, what are you doin'?" And Zeke replied: "Well, I don't rightly know. I've either found a rope—or lost a cow."

Homologous Marrow Transplantation in Rabbits After Triethylenethiophosphoramide

K. A. PORTER and JOSEPH E. MURRAY, M.D., Boston

Triethylenethiophosphoramide (Thio-TEPA), the sulfur derivative of triethylenephosphoramide, has been found to be active in preventing metastases of rat mammary adenocarcinoma.[1] Clinically, temporary regression of human breast carcinoma has also been obtained,[2-4] this drug being one of the few so far discovered with a definite effect on malignant epithelial tumors. However, bone-marrow depression, especially in patients with osseous metastases, has been encountered as a serious toxic effect, limiting the dosage which can be employed.

When marrow aplasia occurs in animals after exposure of the whole body to x-rays, the process can be reversed in some instances by an intravenous injection of homologous myeloid cells, the depleted blood-forming tissues being colonized by cells derived from those which have been injected.[5]

The present experiments were therefore undertaken to determine whether homologous * marrow would similarly implant any proliferate when infused into rabbits which had received marrow-depressant doses of triethylenethiophosphoramide.

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From the Laboratories for Surgical Research, Harvard Medical School and Peter Bent Brigham Hospital.

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Materials and Methods

Animals.—The treated animals were young male New Zealand White rabbits which were not inbred in the genetic sense and weighed 2-2.5 kg. They were housed individually in metal cages. The diet was Purina Laboratory Chow, Supplemented with hay and carrots.

Triethylenethiophosphoramide (Thio-TEPA, Lederle).—A saline solution containing 10 mg. of the substance per milliliter was prepared freshly every six days and stored in a refrigerator. Sterilization was by filtration through fritted glass. Solutions were not used after they were six days old because of the instability of triethylenethiophosphoramide in this state.

X-Irradiation.—Total-body x-irradiation was done with a Phillips machine under the following conditions: 250 kvp; 15 ma., 50 cm. target distance; 0.4 mm. Sn, 0.25 mm. Cu, and 1.0 mm. Al filtration; H. V. L. 2.5 mm. Cu; 50 r per minute dose rate.

Bone Marrow Preparation.—The marrow donors were female New Zealand White rabbits. Marrow was collected from the bones of all four limbs and suspended in saline; then the volume was adjusted so that each 10 ml. contained 1200 ($\times 10^6$) nucleated cells.

Antibiotic Therapy.—Tetracycline hydrochloride (Achromycin soluble) was given in the drinking water, the amount being adjusted so that each animal drank 70-75 mg. of tetracycline per day. Any animal failing to drink or drinking very little received supplemental intramuscular tetracycline to ensure the same total dose of antibiotic.

Hematology.—Total leukocyte and differential counts and hemoglobin and microhematocrit de-

* Homologous: From an individual of different genotype but of the same species; as distinct from isologous: from another individual of the same inbred strain.

Survival of, and Number of Marrow Transplants in, Rabbits Given Triethylenethiophosphoramide (Thio-tepa) Followed by Homologous Bone Marrow

Group		Treatment *	No. of Animals	No. of Animals Surviving Weeks After Starting Thio-TEPA						No. of Marrow "Takes"
				1	2	3	4	5	6	
1	Control	Thio-TEPA 3 mg/kg I. V. ×4	10	10	10	10	10	10	10	0
	Test	Thio-TEPA 3 mg/kg I. V. ×4 + bone marrow	10	9	9	9	9	9	9	0
2	Control	Thio-TEPA 4 mg/kg. I. V. ×4	10	8	7	7	7	7	7	0
	Test	Thio-TEPA 4 mg/kg. I. V. ×4 + bone marrow	10	7	6	6	6	6	6	0
3	Control	Thio-TEPA 5 mg/kg. I. V. ×4	20	12	8	8	8	8	8	0
	Test	Thio-TEPA 5 mg/kg. I. V. ×4 + bone marrow	20	13	11	10	10	10	10	4
4	Control	Thio-TEPA 5 mg/kg. I. V. ×2 + 600 r x-rays	10	8	6	5	5	5	5	0
	Test	Thio-TEPA 5 mg/kg. I. V. ×2 + 600 r x-rays + bone marrow	10	7	6	5	5	5	5	0

* All animals were given tetracycline hydrochloride from the commencement of triethylenethiophosphoramide (Thio-TEPA) administration until two weeks after its cessation.
Bone-marrow dosage: 1200 (×10⁴) nucleated cells in 10 ml. of saline given intravenously.

terminations were made every two days for the first 30 days and once per week thereafter. Blood films were taken at the same time intervals and stained by Wright's method and the heterophils examined for nuclear "drumsticks," as described previously.[6] Before accepting the supposition that the leukocytes were at least in part derived from the transplanted female bone marrow, it was again arbitrarily decided that a minimum of six cells showing typical discrete chromatin nodules should be found. The number of such cells seen in examining 300 heterophils was recorded as a percentage of the heterophil count.

Experimental Groups.—The animals were divided into four groups (Table).

Group 1: The 10 pairs of animals were each given triethylenethiophosphoramide 3 mg/kg. intravenously on four successive days. On the fifth day one member of each pair was given bone marrow intravenously.

Group 2: The 10 pairs of animals in this group each received triethylene thiophosphoramide 4 mg/kg. intravenously on four successive days, followed by bone marrow on the fifth day to one rabbit in each pair.

Group 3: In this group 20 pairs of animals were each given triethylenethiophosphoramide 5 mg/kg. intravenously on four successive days, followed by homologous bone marrow intravenously on the fifth day to one member of each pair.

Group 4: The 10 pairs of male rabbits in this group each received triethylenethiophosphoramide 5 mg/kg. intravenously on two successive days; on the third day each was exposed to 600 r of whole-body x-radiation. Within one hour of the irradiation one animal from each pair was given bone marrow intravenously.

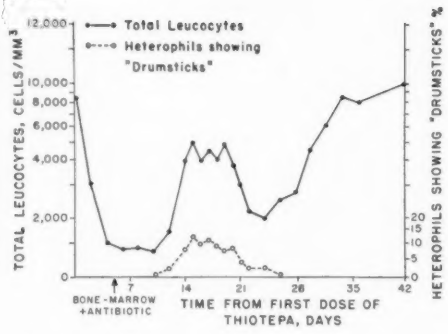
As pilot experiments had shown that animals given triethylenethiophosphoramide were extremely suspectible to massive bacteremia, in these experiments a broad-spectrum antibiotic, tetracycline hydrochloride, was given from the commencement of triethylenethiophosphoramide administration until two weeks after its cessation.

All animals that died were autopsied; sections were prepared and stained with hematoxylin and eosin.

Results

Triethylenethiophosphoramide (Thio-TEPA) in doses of 3 mg/kg. of body weight intravenously given on four successive days proved not too toxic, all the animals after some initial loss of weight regaining their original weight and remaining alive and well for the six-week period they were under observation. There was marked depression of the total leukocyte count, the heterophils being more profoundly depressed than the lymphocytes, and of the platelets. Transfused marrow cells failed to become implanted, as shown by the failure of heterophils from female marrow to appear in the peripheral blood, but there seemed to be no deleterious effect from the marrow administration.

When doses of 4 mg/kg. were used, some of the animals died of hemorrhage in the first 7-10 days. The marrow aplasia was marked and prolonged, regeneration of the animal's own cells causing restoration of the total leukocyte count to commence about the 15th day. Marrow transplantation still failed.



Rejection of initially successful marrow homotransplant in a male rabbit treated with female homologous marrow after toxic doses of triethylenethiophosphoramide (Thio-TEPA).

After a dose of 5 mg/kg. intravenously for four days, many animals died of hemorrhage; some died as the result of toxic complications of the drug, massive liver necrosis and renal damage, resembling necrotizing papillitis, being the most frequent. Depression of the marrow was profound, and autopsy of animals dying in the first two weeks showed an aplastic marrow and marked depletion of lymphocytes from the lymphoid nodules of the spleen, appendix, mesenteric lymph node, and, to a less extent, the thymus. In four animals (20%) there was a successful homotransplant, as indicated by rapid restoration of the total leukocyte count and the appearance of heterophils showing female nuclear sex chromatin (Figure). One of these animals with a successful transplant died at eight days in uremia following necrotizing papillitis. Three rejected the transplant between the 14th and the 28th day; regeneration of their own bone marrow followed, and all survived.

In the last group, in an attempt to avoid the toxic complications of high-dosage triethylenethiophosphoramide, a combination of the drug in sublethal dosage and sublethal whole-body x-irradiation (600 r) was used. The mortality remained high, mainly from hemorrhage; and no successful marrow transplants were recorded.

Comment

These results indicate that highly toxic doses of triethylenethiophosphoramide have to be used to suppress the host's immune mechanism to an extent sufficient to enable successful homologous bone-marrow transplantation. This means that a large percentage of animals die of effects of the drug on systems other than the hematopoietic. In addition, depression of the platelets occurs early, and hemorrhage is a constant hazard until megakaryocytes in the proliferating marrow transplant can restore the platelet count to normal. Furthermore, even at this toxic level, the host's immune system appears to recover rapidly, with resultant rejection of the graft at 14-28 days. These findings are reminiscent of those seen in bone-marrow treatment of animals exposed to total-body x-irradiation in a midlethal dose. Here early rejection of the initially successful graft occurs,[7] but in this instance it is often followed by death of the animal.

It was hoped that a combination of x-irradiation and triethylenethiophosphoramide treatment might overcome these difficulties; but, since bone-marrow transplantation failed, it was presumed that the host's immune responses were still insufficiently depressed.

Sartorelli and LePage[8] have reported treatment of thioguanine marrow depression with isologous and homologous bone marrow intraperitopeally. As a "label" was not used in these studies, it is not known whether cellular transplantation was achieved. Normally the intraperitoneal route is inferior to the intravenous,[9] and much higher doses of marrow are needed to bring about the same effect. This difference would not be so important with isologous tissue, with which there is no immunological problem and few cells are needed to "seed" the depleted host marrow spaces, but homologous marrow given by this route would be less likely to become implanted successfully.

Fisken and associates[10] gave homologous marrow intravenously to busulfan (Myleran)-treated rats and claimed that it caused

reversal of the marrow damage. However, as they also reported that the lymphocytes were apparently unaffected by the busulfan treatment, caution is necessary before postulating marrow homotransplantation as the cause of the beneficial effects.

Summary

Male rabbits were given varying large doses of triethylenethiophosphoramide (Thio-TEPA) intravenously. In all cases marked depression of the bone marrow resulted.

Treatment of this bone-marrow aplasia was attempted by administration of homologous female bone marrow intravenously. Initially successful transplantation, as shown by the appearance of female heterophils in the peripheral blood of the male recipients, was achieved in a few cases.

However, the dosage of triethylenethiophosphoramide necessary to allow this transplantation to occur caused many toxic complications, leading to a high mortality. Furthermore, the homotransplants were rejected before the 28th day, presumably owing to recovery of the host's immune defenses.

Marrow homotransplantation failed to occur after a combination of sublethal doses of triethylenethiophosphoramide and sublethal whole-body x-irradiation.

Dr. F. D. Moore gave suggestions and aid; Dr. S. Farber assisted in obtaining triethylenethiophosphoramide, and Dr. G. J. D'Angio and the x-ray department of the Children's Hospital granted us x-irradiation facilities. The Thio-TEPA used in this investigation was supplied by the American Cyanamid Company.

Department of Surgery, Harvard Medical School (Dr. Murray).

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Distribution of Radioactive Tryptophan in a Patient with Metastatic Carcinoid

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In a previous report [1] attention was called to the direct uptake of radioactive tryptophan by metastatic carcinoid tumor in vivo, demonstrated in a patient known to harbor this tumor prior to laparotomy.

An opportunity to obtain additional data in a similar case was recently afforded us, and it seems worthy of recording these in the light of the rarity of these tumors and their pharmacological significance.

This patient was admitted to the hospital with a diagnosis of small-intestine obstruction. Laparotomy was performed and revealed the presence of a tumor in the terminal ileum which was narrowing the lumen of the small bowel. The tumor and adjacent small bowel were resected and intestinal continuity reestablished. Palpation of the surface of the liver at the time of surgery disclosed a small solitary nodule, thought to represent metastatic tumor. The patient's postoperative course was uneventful, and the pathologist reported the primary tumor to be a carcinoid. It was decided to operate upon the patient again and remove the apparently solitary nodule from the liver.

Method

Five hours prior to surgery the patient received 25μc. of C^{14} tryptophan orally. At surgery the nodule, which proved to be metastatic carcinoid, was removed and biopsy specimens of normal liver, skeletal muscle, and rectal mucosa were also obtained. Following tissue oxidation these specimens were assayed for their C^{14} activity, using a flow-type Geiger counter. The results of these studies are shown in the Table.

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Departments of Surgery and Pediatrics, University Hospitals of Cleveland and Western Reserve University School of Medicine.

β-C^{14}-DL-Tryptophan Uptake

Tissue	Counts per Min/Mg. Dry Wt.
Carcinoid tumor	1205
Skeletal muscle	1.0
Liver	2.6
Rectal mucosa	5.0

Results

These findings are in agreement with the previous study and show a high uptake of the carbon-labeled tryptophan by the metastatic carcinoid tumor.

Comment

This study supports Udenfriend's [2] description of the metabolic pathway of tryptophan in patients with carcinoid tumors and testifies to the fact that these tumors have an avidity for this essential amino acid. The uptake of the tryptophan by the tumor is not surprising in view of the fact that carcinoids are known to contain large quantities of serotonin,[3] a substance whose precursor presumably is tryptophan.

Summary

Radioactive tryptophan administered orally to a patient with metastatic carcinoid was found to localize in the tumor, as demonstrated by direct C^{14} assay of the tumor removed at surgery. The uptake by the tumor was much greater than that noted in normal rectal mucosa, liver, or skeletal muscle.

Drs. T. N. Cline and K. M. Brownson, of Traverse City, Mich., cooperated in this study.

Dept. of Surgery, University Hospitals of Cleveland. A. E. C. Contract #W-31-109-eng-78.

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Fifteen-Year Study of Anesthesia for 6301 Cases of Thoracic Surgery

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Intrathoracic surgical procedures of the greatest complexity are performed today in most large hospitals throughout the world, and the number of such procedures is increasing steadily from year to year. One of the major reasons for this increase lies in the increasing availability of anesthesiologists.

There is probably no major field of anesthesiology which requires as much knowledge and skill as the one dealing with anesthesia for thoracic surgery. The physiological and pathological problems encountered in this specialized area are distinct and highly complex. The respiratory and circulatory complications, both during and following the surgical procedure, are frequently of grave prognostic significance, and the role of the anesthesiologist in the prevention and treatment of these complications can hardly be overemphasized.

In view of such increasing interest in anesthesia for thoracic surgery, it would seem pertinent to present the information obtained and the observations made in connection with the administration of 6301 anesthetics for thoracic operations during a period of 15 years. These observations were gathered by the members of the department of anesthesiology of the University of Wisconsin Medical School from 1941 to 1955 inclusive. During this time, and, indeed, ever since 1933 until the present day, every anesthetic administered at the University Hospitals is recorded in full detail by the physician anesthesiologist on the anesthetic chart. This information is later transferred to IBM punch cards, and these cards are maintained as a permanent record. The data coded on these cards include information about the patient, e. g., age, sex, physical status, and preoperative pathology; the nature of the operative procedure; the anesthetic agent or agents used, the technique of administration, the duration of anesthesia; anesthetic and surgical complications during or after the operation; treatment during the operation and postoperatively, and a number of other data of relatively minor importance. The coding and punching of every card were personally supervised, until the day of his untimely death, in August, 1955, by Dr. Noel A. Gillespie, thus providing homogeneity and a uniform approach to the difficult and frequently misleading problem of medical record keeping.

A detailed history of the development of thoracic surgery and of anesthesia for thoracic surgery lies beyond the scope of this paper. Suffice it to say that, after a cautious and relatively slow beginning, most of the basic surgical techniques reached their present state of high accomplishment by the late 1940's. It was also shortly after this time that the introduction of muscle-relaxant drugs into clinical anesthesiology facilitated the hitherto rather formidable procedure of endotracheal intubation and provided the anesthesiologist with the new, and increasingly popular, technique of nitrous oxide-thiobarbiturate-curare anesthesia. An attempt will be made later in this series of papers to indicate the effects

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TABLE 1.—*Types and Totals of Thoracic Operative Procedures from 1941 to 1955 Inclusive*

For postoperative hemostasis	15
Repair of penetrating wounds	13
Empyema drainage	145
Exploration, inoperable	411
Open pneumolysis	6
Cavernostomy	48
Decortication	91
Segmental resections and lobectomies	1691
Pneumonectomy	495
Pericardiectomy	22
Ligation, patent ductus arteriosus	125
Repair of coarctation of aorta	48
Repair of tetralogy of Fallot	38
Mitral valvulotomy	65
Repair of diaphragmatic hernia	105
Esophagectomy	89
Esophagoplasty	44
Transthoracic gastrectomy	43
Excision of mediastinal tumors	69
Miscellaneous intrathoracic operations	328
Thoracoplasties	2022
Other extrapleural procedures	391
Total	6301

of this and of other changes in the approach to the problem of anesthesia for thoracic surgery.

All anesthetics in this series were administered by the members of the department of anesthesiology at the University Hospitals. Only the staff anesthesiologists and residents of advanced standing, under direct staff supervision, were permitted to anesthetize patients for thoracic surgery. The surgical procedures were performed by staff surgeons or by surgical residents in their last year of training.

In this paper the over-all experiences with the entire series of 6301 cases will be presented. In a second paper, we shall discuss, in much greater detail, the experiences with 2186 cases of pulmonary resection, including the postoperative respiratory and circulatory complications. A third paper will deal with the mortality which occurred in the group of patients in whom pulmonary resection was performed. It is not our intention to compare our results with those reported from other institutions. Such comparisons are, at best, on very tenuous grounds, and we feel that a simple presentation of data, with perhaps a few explanatory notes, will suffice to accomplish our purpose.

During the 15 years under discussion (1941-1955) a total of 6301 thoracic surgical procedures were performed. The types of and totals for the operations performed are indicated in Table 1. It can be noted that the most numerous procedures were thoracoplasty, segmental resection of the lung, or lobectomy, and pneumonectomy. In 411 instances inoperable tumors were found. There were 298 operations on the heart and pericardium. The annual distribution of the various major groups of operations is presented in Table 2. It is apparent from this Table that the number of pulmonary resections increased rapidly until 1953 and then declined slightly from the 387, in that year, to 241, in 1955. Thoracoplasties reached their peak in 1946, and, except for a secondary peak in 1949, have declined slowly thereafter. The patients on whom these 6301 procedures were performed ranged in age from the first day of life to 86 years, with the large majority between 30 and 50 years.

TABLE 2.—*Types of Thoracic Operations Performed by Year from 1941 to 1955 Inclusive*

	Thoraco-plasties	Pulmonary Resections	Mediastinal Procedures	Operations on the Esophagus	Cardiac Operations	Other Intra-thoracic Procedures	Miscella-neous	Totals
1941	84	11	0	5	3	36	36	175
1942	171	7	0	2	6	16	66	268
1943	239	5	0	4	2	27	42	319
1944	222	9	0	0	1	61	26	319
1945	214	33	3	2	3	73	32	360
1946	269	46	1	3	9	57	31	416
1947	164	85	3	9	19	60	20	360
1948	141	145	5	5	9	102	14	421
1949	204	130	8	6	34	79	12	473
1950	155	183	7	25	22	83	21	496
1951	45	270	6	7	35	81	19	463
1952	23	330	8	11	28	93	28	521
1953	34	387	7	15	56	93	19	611
1954	26	304	14	12	75	134	22	587
1955	31	241	7	18	59	129	27	512
	2022	2186	69	124	361	1124	415	6301

TABLE 3.—*Distribution by Physical Status of 6301 Patients Having Thoracic Operations in Fifteen Years of Study*

	Elective										Emergency				
	1 Good		2 Fair		3 Poor		4 Bad		5 Good		6 Poor		7 Moribund		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	Total
1941	8	4.5	101	57.7	56	32.0	6	3.4	0		4	2.2	0		175
1942	3	1.1	139	51.8	113	42.1	9	3.3	1	0.3	0		3	1.6	268
1943	8	2.5	177	55.5	132	41.3	1	0.3	0		1	0.3	0		319
1944	4	1.2	118	37.0	190	59.5	6	1.8	0		1	0.3	0		319
1945	3	0.8	143	39.7	200	55.5	7	1.9	3	0.8	3	0.8	1	0.3	360
1946	8	1.9	228	54.8	175	42.0	3	0.7	0		2	0.5	0		416
1947	13	3.6	196	54.4	140	38.9	6	1.6	2	0.6	1	0.3	2	0.6	360
1948	7	1.6	196	46.5	198	47.0	7	1.6	2	0.5	11	2.6	0		421
1949	8	1.7	226	47.8	226	47.8	7	1.4	3	0.6	2	0.4	1	0.2	473
1950	16	3.2	237	47.8	224	45.1	13	2.6	0		6	1.2	0		496
1951	20	4.3	275	59.4	142	30.6	13	2.8	0		11	2.3	2	0.4	463
1952	14	2.6	272	52.2	205	39.3	16	3.0	0		13	2.5	1	0.2	521
1953	15	2.4	388	63.5	181	29.6	13	2.1	1	0.1	12	2.0	1	0.1	611
1954	16	2.7	290	49.4	231	39.3	27	4.6	2	0.3	17	2.8	4	0.7	587
1955	12	2.3	224	43.7	219	42.7	34	6.6	0		19	3.7	4	0.8	512
	155	2.5	3210	51.0	2632	41.8	168	2.7	14	0.3	103	1.7	19	0.4	6301

The physical status of these patients is given in Table 3. The large majority, 92.8%, are in Group 2 (fair status), or Group 3 (poor status), with no significant change in the physical status distribution over the years of the study. The number of patients of the best (good) and that of the poorest (bad) status for elective procedures were essentially the same. The total of all procedures of an emergency nature, or on moribund patients, was practically the same (2.4%) as the totals for the good and the bad group.

The principal anesthetic agents used during these procedures are shown in Table 4. It is most interesting to note that cyclopropane dominated the field through 1947. It was replaced by ether, which, in turn, gave way to nitrous oxide and its adjuvants by 1953. Chloroform, ethylene, and regional anesthetic agents were used in a relatively small number of cases, and their use usually reflects the interest shown in these agents by individuals.

The anesthetic techniques used are summarized in Table 5. The marked increase in the use of endotracheal techniques after 1946 coincided with the increase in pulmonary resections. Endotracheal techniques also increased greatly within two to three years after the introduction of the curariform drugs into clinical anesthesiology. In the large majority of all inhalation anes-

TABLE 4.—*Principal Anesthetic Agents Used in 6301 Thoracic Operations*

	Cyclopropane		Ether		Nitrous Oxide and Adjuvants		Chloroform		Regional		Miscellaneous Inhalational Agents *	Totals
	No.	%	No.	%	No.	%	No.	%	No.	%		
1941	136	77.7	2	1.1	14	7.9	5	2.8	4	2.2	12	175
1942	228	85.0	8	2.9	5	1.8	7	2.6	9	3.3	11	268
1943	219	68.6	25	7.8	14	4.3	47	14.7	1	0.3	13	319
1944	187	58.6	15	4.7	14	4.3	24	7.5	60	18.0	19	319
1945	227	63.0	26	7.2	13	3.6	42	11.6	39	10.8	3	360
1946	336	80.7	30	7.2	8	1.9	36	8.6	0		6	416
1947	212	58.8	125	34.7	6	1.6	8	2.2	0		9	360
1948	132	31.3	268	63.6	2	0.5	15	3.5	3	0.7	1	421
1949	151	31.9	311	65.7	8	1.6	1	0.2	1	0.2	1	473
1950	61	12.2	428	86.2	5	1.0	1	0.2	1	0.2	0	496
1951	83	17.9	361	77.9	19	4.1	0		0		0	463
1952	106	20.3	325	62.3	67	12.8	9	1.7	13	2.4	1	521
1953	22	3.6	145	23.7	418	68.3	3	0.5	12	2.0	11	611
1954	81	13.7	145	24.7	352	59.9	0		3	0.8	6	587
1955	36	7.0	138	26.9	322	62.8	2	0.35	5	1.0	9	512
	2217	35.2	2352	37.3	1267	20.1	200	3.2	151	2.4	102 1.6%	6301

* Miscellaneous inhalation agents include ethylene, divinyl ether (Vinethene), ethylvinyl ether (Vinamar), and trifluoroethylvinyl ether (Fluoromar).

TABLE 5.—*Summary of Anesthetic Techniques Used in 6301 Thoracic Operations*

	Inhalation Nonendotracheal		Inhalation Endotracheal		Intravenous		Regional		
	No.	%	No.	%	No.	%	No.	%	Totals
1941	99	56.57	64	36.57	8	4.57	4	2.28	175
1942	194	72.38	54	20.15	11	4.10	9	3.35	268
1943	264	82.75	48	15.04	6	1.88	1	0.31	319
1944	210	65.85	48	15.04	1	0.31	60	18.80	319
1945	246	68.33	71	19.72	4	1.11	39	10.83	360
1946	297	71.39	118	28.36	1	0.24	0		416
1947	194	53.89	164	45.55	2	0.55	0		360
1948	163	38.72	255	60.57	0		3	0.72	421
1949	216	45.66	255	53.91	1	0.21	1	0.21	473
1950	154	31.05	341	68.75	0		1	0.20	496
1951	30	6.48	433	93.52	0		0		463
1952	12	2.30	496	95.20	0		13	2.50	521
1953	13	2.12	586	95.90	0		12	1.96	611
1954	19	3.23	564	96.08	1	0.17	3	0.51	587
1955	11	2.15	496	96.87	0		5	0.97	512
	2122	33.67	3993 *	63.37	35	0.55	151	2.39	6301

* In 34 cases anesthesia was endobronchial.

TABLE 6.—*Duration of Anesthesia, in Minutes, in 6301 Thoracic Operations in the Fifteen-Year Survey*

	Duration of Anesthesia, Min.									Total No. Cases
	30	30–60	60–90	90–120	120–180	180–240	240–300	300	Average	
1941	23	61	39	28	19	4	0	1	91.3	175
1942	23	83	89	43	23	3	4	0	94.1	268
1943	34	139	100	21	14	7	4	0	82.3	319
1944	48	125	85	31	13	8	9	0	85.4	319
1945	46	121	101	34	31	20	7	0	95.0	360
1946	29	147	126	45	48	17	3	1	97.2	416
1947	26	121	67	27	77	33	6	3	116.8	360
1948	19	75	90	66	112	53	5	1	132.7	421
1949	11	84	91	90	118	60	13	6	134.3	473
1950	2	59	71	93	155	91	20	5	158.7	496
1951	2	37	90	92	178	48	10	6	151.9	463
1952	7	33	77	119	219	55	9	2	152.6	521
1953	9	28	139	190	185	42	14	4	141.4	611
1954	10	31	82	147	208	71	24	14	160.7	587
1955	1	20	49	81	147	112	51	51	202.9	512
	290	1164	1296	1107	1547	624	179	94		6301

TABLE 7.—*Blood Transfusions During Anesthesia for Thoracic Procedures*

	No. of Patients Receiving Blood	Total Cases	Percentage
1941	13	175	7.4
1942	15	268	5.6
1943	10	319	3.1
1944	23	319	7.2
1945	54	360	15.1
1946	90	416	21.6
1947	149	360	41.4
1948	251	421	59.6
1949	274	473	58.0
1950	373	496	75.4
1951	381	463	82.3
1952	455	521	87.4
1953	522	611	85.5
1954	479	587	81.8
1955	404	512	79.1
	3493	6301	55.2

TABLE 8.—*Incidence of Death in 6301 Thoracic Operations by Year*

	Deaths	Total Cases	Percentage Deaths
1941	11	175	6.3
1942	10	268	3.7
1943	12	319	3.8
1944	24	319	7.5
1945	10	360	2.8
1946	19	416	4.6
1947	22	360	6.1
1948	20	421	4.8
1949	24	473	5.1
1950	19	496	3.8
1951	30	463	6.5
1952	27	521	5.2
1953	34	611	5.6
1954	40	587	6.8
1955	35	512	6.8
	337	6301	5.35%

thetic administrations in this series the "to-and-fro" technique was employed.

The duration of anesthesia and the average time for all anesthetics administered are shown, in minutes, in Table 6. The times given were determined from the beginning of induction until the time at which the patient is taken from the operating room at the conclusion of the operation. The increasing length of anesthesia, particularly after 1946, indicates the increasing complexity of the operative procedures, the introduction of cardiac surgery, and the increasing participation of surgical residents in performing major thoracic operations.

The number of patients who received one or more units of whole blood while in the operating room is indicated in Table 7. The steadily increasing use of blood administered during operations reflects increased awareness of the importance of adequate and early blood replacement, increased availability of blood, and the need of support of the patient with the increasing length of thoracic surgical procedures.

The incidence of death in this series of 6301 patients is given in Table 8. The totals include all patients who died during their hospital stay following thoracic surgery. Since it is frequently difficult, and occasionally impossible, to determine the precise cause of death, no attempt is made to distinguish between the groups of patients whose death could, arbitrarily, be classified as being due to anesthetic, surgical, or other unrelated causes. The relatively high percentages in the last five years probably are due to more difficult cardiac procedures which are being performed.

Summary

A 15-year study of anesthesia for 6301 cases of thoracic surgical procedures from 1941 to 1955, inclusive, is presented. The data are tabulated on the basis of annual distribution, the physical status of the patients, the principal anesthetic agent used, the anesthetic technique, the duration of anesthesia, and the over-all mortality.

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A Fifteen-Year Study of Anesthesia for 2186 Cases of Pulmonary Resection

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The first paper in this series presented our experiences with 6301 cases of anesthesia for all types of thoracic surgery. This paper will present in greater detail observations on the 2186 patients undergoing pulmonary resection. In selecting these patients from the total number of cases, we wished to choose a group which was comparable on the basis of the operation performed, and in which we could compare some of the factors influencing postoperative morbidity. The group includes patients having segmental resections, lobectomy, and pneumonectomy, but not those for whom such a procedure had been proposed but found not possible at the time of operation. A third paper will discuss the incidence of death in this same selected group of patients.

The distribution of pulmonary resections during the 15 years of this study is presented in Table 1. More than half of these operations were performed during the last five years.

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TABLE 1.—*Number of Pulmonary Resections Each Year from 1941 to 1955, Inclusive*

1941	11
1942	7
1943	5
1944	9
1945	33
1946	46
1947	85
1948	145
1949	130
1950	183
1951	270
1952	330
1953	387
1954	304
1955	241
	2186

The principal anesthetic agent used in each of these 2186 cases of pulmonary resection is shown in Table 2. It is of interest to note the trend from cyclopropane, used primarily during the first five years of the study, to ether, used during the second five years, to nitrous oxide and its adjuvants, employed during the last five years of the study. This last phase reflects the availability of muscle-relaxant drugs in clinical anesthesiology. In all but three of the patients an endotracheal technique was

TABLE 2.—*Principal Anesthetic Agents Used Each Year in Pulmonary Resections*

	Cyclopropane	Ether	Nitrous Oxide	Chloroform	Regional	Misc.	Total
1941	11	0	0	0	0	0	11
1942	6	1	0	0	0	0	7
1943	5	0	0	0	0	0	5
1944	5	2	0	0	2	0	9
1945	16	6	0	3	8	0	33
1946	38	7	0	1	0	0	46
1947	19	64	0	1	0	1	85
1948	1	139	0	4	1	0	145
1949	1	127	2	0	0	0	130
1950	7	172	4	0	0	0	183
1951	42	218	10	0	0	0	270
1952	49	114	153	5	9	0	330
1953	5	62	306	3	9	2	387
1954	20	63	221	0	0	0	304
1955	7	30	204	0	0	0	241
	232	1005	900	17	29	3	2186

TABLE 3.—*Opiate Premedication by Year in 2186 Pulmonary Resections*

	Morphine	Meperidine	Other	Total Opiate Cases	Total Cases	Percentage Opiate Cases
1941	10	0	0	10	11	91.0
1942	6	0	0	6	7	85.8
1943	5	0	0	5	5	100.0
1944	9	0	0	9	9	100.0
1945	10	0	2	12	33	36.4
1946	5	0	0	5	46	10.9
1947	1	0	0	1	85	1.9
1948	2	0	1	3	145	2.1
1949	10	0	0	10	130	7.7
1950	63	11	0	74	183	40.5
1951	56	1	3	60	270	22.3
1952	40	26	8	74	330	22.4
1953	36	241	2	279	387	72.2
1954	104	137	32	273	304	89.9
1955	175	49	10	234	241	96.9
	532	465	58	1055	2186	50.6

used, and in the very large majority of all cases a "to-and-fro" method was employed.

Table 3 indicates the use of opiates in preliminary medication. The marked decline in the use of these drugs from 1945 to 1952 reflects the feeling prevalent in that period that less circulatory and respiratory depression would occur during and after the operative procedure if belladonna alkaloids only were used as preliminary medication. With increasing use of nitrous oxide anesthesia in 1952 and after, a marked increase in the preoperative use of opiates again is evident.

TABLE 4.—*Blood Transfusions During Anesthesia in 2186 Pulmonary Resections*

	Blood	Total Cases	Percentage
1941	5	11	45.5
1942	3	7	42.8
1943	3	5	60.0
1944	8	9	88.9
1945	30	33	90.9
1946	41	46	89.1
1947	79	85	92.9
1948	141	145	97.2
1949	128	130	98.5
1950	173	183	94.5
1951	259	270	95.9
1952	323	330	97.9
1953	350	387	90.4
1954	284	304	93.4
1955	226	241	93.8
	2053	2186	93.9

The use of whole blood during the operative procedure may be seen in Table 4. During the last 12 years the percentage of patients receiving one or more units of whole blood while in the operating room has varied only slightly.

The complications occurring during anesthesia are shown, on an annual basis, in Table 5. The satisfactoriness of the anesthetic administration was determined by the individual responsible for it. It is of interest to note that, although a relatively large number of anesthesiologists have contributed cases to this series, the percentage distribution of satisfaction has varied but slightly during the 15-year period of our study.

TABLE 5.—*Complications During Anesthesia in 2186 Pulmonary Resections*

	None	Deficient Relaxation	Other Surg. Dissatisfact.	Obstruction or Hypoxia	Other Anes. Dissatisfact.	Unsatisfact. to Patient	Ineptitude	Total Cases
1941	8(72.7)*	0	1	2	0	0	0	11
1942	5(71.4)	0	0	1	1	0	0	7
1943	3(60.0)	0	0	0	2	0	0	5
1944	6(66.7)	0	0	2	1	0	0	9
1945	21(63.6)	0	1	1	11	1	0	33
1946	39(84.8)	0	3	2	4	4	0	46
1947	71(83.5)	1	2	5	5	2	3	85
1948	121(83.4)	1	3	8	11	2	10	145
1949	114(87.7)	2	3	7	3	1	3	130
1950	157(85.8)	2	2	11	4	2	5	183
1951	237(87.8)	4	3	12	13	1	9	270
1952	303(91.8)	4	3	3	8	3	10	330
1953	369(95.3)	1	2	5	5	2	6	387
1954	274(90.1)	3	5	10	4	1	13	304
1955	222(92.1)	1	1	6	9	0	3	241
	1950(88.4)	19	29	75	81	19	62	2186

* Figures in parentheses are percentages.

TABLE 6.—*Postoperative Circulatory Complications After 2186 Pulmonary Resections*

	Emboli	Circ. Failure	Coronary Disease	Arrhythmia	Circulatory Depression (Shock)	Hemorrhage	Hypotension, Severe	Total Circ. Complications	Total Cases	Percentage Complications
1941	0	0	0	1	0	0	0	1	11	9.1
1942	0	1	0	1	1	0	2	5	7	71.4
1943	0	0	0	1	0	1	2	4	5	80.0
1944	0	0	0	0	1	0	1	2	9	22.2
1945	0	0	0	2	2	2	8	14	33	42.4
1946	0	1	0	2	2	0	8	13	46	28.3
1947	0	2	0	18	4	0	14	38	85	44.8
1948	1	3	0	9	1	1	8	23	145	15.9
1949	0	1	0	21	0	2	8	32	130	24.6
1950	2	0	0	23	1	3	8	37	183	20.3
1951	1	4	0	15	1	6	5	32	270	11.9
1952	1	0	1	11	1	8	3	25	330	7.6
1953	5	2	0	5	1	4	6	23	387	5.9
1954	4	3	1	23	2	5	8	46	304	15.1
1955	1	0	1	18	2	8	4	34	244	14.2
	15	17	3	150	19	40	85	329	2186	15.1

Postoperative Morbidity

Owing to the nature of the preexisting pathology and of the surgical procedure, postoperative circulatory and respiratory complications may be anticipated with greater frequency after pulmonary resections than after most other types of operations. Parts of the remaining lung tissue may be involved in the disease process; there may be mechanical disturbances limiting normal ventilation; pleural effusion may compress normal lung tissue, and the postoperative pain may limit the patient's ability to cough and to remove the accumulated secretions from the tracheobronchial tree. These and other factors produce conditions favorable to the development of circulatory and respiratory complications.

The postoperative *circulatory complications* were grouped into seven classes.

1. Emboli
2. Circulatory failure
3. Coronary disease—infarction, thrombosis
4. Cardiac arrhythmias
5. Circulatory depression, shock
6. Hemorrhage
7. Severe hypotension

The distribution of these circulatory complications by year is shown in Table 6. Cardiac arrhythmias occurred in 6.9%, severe hypotension in 3.9%, and hemorrhage in 1.8%, of the 2186 cases. None of the other postoperative circulatory complications occurred with even 1% frequency.

Because of the small number of many of these complications and for the sake of simplicity, all circulatory complications were analyzed together on the basis of the patient's age, the physical status, the duration of anesthesia, and the principal anesthetic agent used. The complications according to the patient's age are tabulated in Table 7. It is apparent that these complications are high in the first decade of life and increase sharply again after the age of 50.

The incidence of circulatory complications according to the patient's physical status is shown in Table 8. The finding that patients in poor physical condition have more postoperative circulatory complications is not surprising.

The incidence of circulatory complications with increasing duration of anesthesia is presented in Table 9. The sharp increase in postoperative circulatory morbidity following procedures of more than three

TABLE 7.—*Postoperative Circulatory Complications by Age Following 2186 Pulmonary Resections*

Age, Yr.	0–1	1–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80+	Total
Complications	0	9	14	69	67	49	65	48	8	0	329
Total Cases	3	42	147	515	505	436	311	194	31	2	2186
Percentage	0	21.5	9.5	13.4	13.2	11.3	20.9	24.8	25.8	0	15.1

TABLE 8.—*Incidence of Postoperative Circulatory Complications by Physical State in 2186 Pulmonary Resections*

	Elective				Emergency			
	1 Good	2 Fair	3 Poor	4 Bad	5 Good	6 Poor	7 Moribund	Total
Complications	3	158	160	7	0	0	1	329
Total Cases	21	1376	762	21	1	3	2	2186
Percentage	14.3	11.5	21.0	33.3	0.0	0.0	50	15.1

hours' duration is due, in part, to the fact that patients with more advanced pathological conditions usually require a more extensive, and thus longer, surgical procedure. We do feel, however, that the duration of anesthesia in itself must also contribute to the increase of postoperative circulatory complications.

In Table 10 the circulatory complications are tabulated on the basis of the principal anesthetic agent used. The large number of complications following cyclopropane and ether anesthesia as compared with the relatively small number of such complications with thiobarbiturate-nitrous oxide-curare anesthesia is very striking. The fact that cyclopropane was used most extensively during the early years of the study and the fact that both cyclopropane and ether have been, on occasion, selected for the poorest-risk patients may explain, to some extent, the disproportionately high incidence of complications following the use of these two agents. The incidence of complications following the use of a muscle-relaxant agent was also examined. A total of 1218 patients were given a muscle-relaxant agent during anesthesia, and 120 of these patients (9.9%) developed postoperative circulatory complications. Among the 968 patients who had no muscle-relaxant drug, 209, i. e., 21.6%, developed circulatory complications. It must be remembered that these agents were not used in anesthesia for thoracic surgery at this institution until about 1949, and thus were not a factor during the early years of this study. The significantly lower incidence of circulatory complications following the use of curare is, nevertheless, very impressive.

TABLE 9.—*Postoperative Circulatory Complications as Related to Duration of Anesthesia, in Minutes, After Pulmonary Resection*

Minutes	30-60	60-90	90-120	120-180	180-240	240-300	Over 300	Total
Complications	0	5	46	145	100	24	9	329
Total Cases	17	156	426	1032	412	104	39	2186
Percentage	0	3.2	10.8	14.1	24.3	23.1	23.1	15.1

The postoperative *respiratory complications* were grouped into six classes.

1. Upper respiratory complications, such as upper respiratory infections, laryngitis, tracheitis, etc.
2. Lower respiratory obstruction—aspiration, hemorrhage, edema, and pneumonia
3. Atelectasis
4. Complications related to the surgical procedure—bronchopleural fistula, pneumothorax, paradoxical respiration, pleural effusion, and empyema
5. Anoxia
6. Tuberculous pneumonia and spread of tuberculosis

TABLE 10.—*Incidence of Postoperative Circulatory Complications Related to Principal Anesthetic Agent Used*

	Chloroform	Cyclopropane	Ether	N_2O-Curare-Barb.	Regional	Total*
Complications	2	56	190	77	3	329
Total	17	232	1005	900	29	2186
Percentage	11.8	24.2	18.9	8.6	10.3	15.1

* There was also one complication following three anesthetics with miscellaneous agents.

TABLE 11.—*Distribution of Postoperative Respiratory Complications Each Year Following 2186 Pulmonary Resections*

	Upper Respiratory	Lower Respiratory	Atelectasis	Operative	Anoxia	Tuberculous Pneumonia and Spread	Total Complications	Total Cases	Percentage
1941	2	1	2	2	0	1	8	11	72.8
1942	1	0	2	3	0	0	6	7	85.9
1943	0	0	1	1	1	0	3	5	60.0
1944	0	1	2	1	0	0	4	9	44.5
1945	1	0	5	5	0	0	11	33	33.3
1946	3	1	2	3	1	0	10	46	21.7
1947	5	1	7	16	1	0	30	85	35.3
1948	7	2	12	17	0	2	40	145	27.7
1949	7	2	13	16	0	3	41	130	31.6
1950	27	4	22	12	0	1	66	183	32.8
1951	8	5	47	55	0	2	117	270	43.4
1952	16	7	36	22	3	1	85	330	25.8
1953	8	5	20	17	3	2	55	387	14.2
1954	18	4	13	8	0	2	45	304	14.9
1955	14	3	19	21	1	1	59	241	24.5
	117(5.4%)	36(1.7%)	203(9.3%)	199(9.1%)	10(0.5%)	15(0.7%)	580	2186	26.6

When more than one postoperative respiratory complication was recorded for any patient, the most significant one was tabulated, so that each patient was included only once.

The annual distribution of these postoperative respiratory complications can be seen in Table 11. A decrease in the incidence in almost all groups can be observed during the last four years. Since the totals in Groups 2, 5, and 6 are very small, and show little variation over the years, these groups have been combined with Group 1 in the following Tables. Thus, the respiratory complications will be analyzed under three headings; i. e., atelectasis, surgical complications, and other complications.

The incidence of respiratory complications on the basis of the patient's age is shown in Table 12. It is rather surprising to note that there is no great relationship between the incidence of postoperative respiratory complications and the patient's age. There were complications in slightly

TABLE 12.—*Distribution of Postoperative Respiratory Complications by Age in 2186 Pulmonary Resections*

	Age, Yr.										
	0–1	1–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80+	
Atelectasis	0	5	25	45	42	38	31	12	5	0	203
Percentage		11.5	17.0	8.7	7.5	11.2	9.9	8.8	9.7		9.3
Surgical	0	7	10	45	38	49	30	17	3	0	199
Percentage		16.3	6.8	8.7	7.5	11.2	9.9	8.8	9.7		9.1
Others	1	3	12	33	40	33	23	31	1	1	178
Percentage	33.3	7.2	8.2	6.4	7.9	7.6	7.4	16.0	3.2	50.0	8.3
Total resp. complications	1	15	47	123	120	120	84	60	9	1	580
Total Cases	3	42	147	515	505	436	311	194	31	2	2186
Percentage	33.3	35.7	32.0	23.9	23.7	27.5	27.0	31.0	29.0	50.0	26.6

TABLE 13.—*Distribution of Postoperative Respiratory Complications by Physical State of Patient in 2186 Pulmonary Resections*

	Elective				Emergency			
	1 Good	2 Fair	3 Poor	4 Bad	5 Good	6 Bad	7 Moribund	Total
Atelectasis	1	119	79	4	0	0	0	203
Percentage	4.8	8.7	10.4	19.2				9.3
Surgical	3	127	66	3	0	0	0	199
Percentage	14.2	9.3	8.7	14.2				9.1
Others	2	82	86	6	1	1	0	178
Percentage	9.5	6.0	11.3	28.6	100	33.3	0	8.3
Total complications	6	328	231	13	1	1	0	580
Total cases	21	1376	762	21	1	3	2	2186
Percentage	28.6	24.3	30.3	61.9	100	33.3	0	26.6

TABLE 14.—*Postoperative Respiratory Complications as Related to Duration of Anesthesia, in Minutes*

Minutes	30–60	60–90	90–120	120–180	180–240	240–300	Over 300	Total
Atelectasis	1	7	37	101	42	11	4	203
Percentage	5.9	4.5	8.7	9.8	10.1	10.6	10.1	9.3
Surgical	1	8	32	110	37	8	3	199
Percentage	5.9	5.1	7.5	10.6	9.0	7.7	7.7	9.1
Others	1	6	25	77	55	11	3	178
Percentage	5.9	3.9	5.8	7.5	13.4	10.6	7.7	8.3
Total complications	3	21	94	288	134	30	10	580
Total cases	17	156	426	1032	412	104	39	2186
Percentage	17.8	13.5	22.1	26.9	32.6	28.8	25.7	26.6

over 30% until the third decade of life and after the seventh decade, but respiratory complications of over 20% appeared in all decades of life.

The effects of physical status on the incidence of postoperative respiratory complications are presented in Table 13. The incidence of atelectasis follows the expected pattern and is highest in those patients whose physical status is the poorest. The incidence of complications related to the surgical intervention appears to be independent of the patient's physical status and varies but little among the groups.

The incidence of respiratory complications tabulated on the basis of the duration of anesthesia is shown in Table 14. The largest number of complications seem to follow operations lasting three to four hours, and a definite increase is evident in all operations lasting longer than 90 minutes.

The effect of the principal anesthetic agent used on the incidence of postoperative respiratory complications is presented in Table 15. The consistently highest incidence of respiratory complications following ether anesthesia and the almost equally high percentage following cyclopropane anesthesia are very interesting. The fact that these two agents were used primarily during the earlier years of the study and the fact that they are, on occasion, selected for the poorest-risk patients may explain, to some extent, why thiobarbiturate-nitrous oxide-curare anesthesia is followed by such a strikingly lower incidence of respiratory complications.

The incidence of respiratory complications following the administration of muscle-relaxant agents was examined. A total of 1218 patients were given a muscle-relaxant agent during anesthesia, and 280 of these patients (22.0%) developed postoperative respiratory complications. In all, 968 patients received no muscle-relaxant drug; yet 300 of these (31.1%) developed respiratory complications. It must be noted again that these agents were not used during the early years of the study. The consistently lower incidence of respiratory complications following the use of muscle-relaxant drugs, however, is highly impressive.

The relationship between preoperative pathology and postoperative respiratory

TABLE 15.—*Incidence of Postoperative Respiratory Complications Related to Principal Anesthetic Agent Used in 2186 Pulmonary Resections*

	Chloroform	Cyclopropane	Ether	Nitrous Oxide	Miscellaneous Agents	Total
Atelectasis	2	25	128	46	2	203
Percentage	11.8	10.4	12.7	5.2	6.9	9.3
Surgical	0	16	140	40	3	199
Percentage	0	6.9	13.9	4.4	10.2	9.1
Others	1	23	104	48	2	178
Percentage	5.9	9.9	10.3	5.3	6.9	8.3
Total complications	3	64	372	134	7	580
Total cases	17	232	1005	900	32	2186
Percentage	17.6	27.7	36.8	14.9	21.9	26.6

TABLE 16.—*Incidence of Postoperative Respiratory Complications Relative to Type of Preexisting Disease in 2186 Pulmonary Resections*

	Total	Postoperative Resp. Complications	Percentage
Carcinoma	272	63	23.2
Tuberculosis	1448	346	23.9
Bronchiectasis	290	105	36.2
Emphysema	10	7	70.0
Adenoma	23	6	26.1
Cyst	13	5	38.5
Atelectasis	19	5	26.3
Hemorrhage	2	1	50.0
Abscess	42	27	64.3
Empyema	10	2	20.0
Miscellaneous	51	8	15.7
None given	6	5	83.3
Total	2186	580	26.6

complications is indicated in Table 16. It is apparent that patients suffering from pulmonary emphysema or lung abscess have a considerably higher incidence of postoperative respiratory complications than patients belonging in any of the other groups. This finding seems to substantiate our clinical impression that pulmonary emphysema is of grave prognostic significance in patients undergoing pulmonary resection.

Summary

A 15-year study of anesthesia in 2186 cases of pulmonary resection is presented. The data are analyzed on the basis of annual distribution, the principal anesthetic agent used, the preliminary medication, and the complications occurring during anesthesia. The postoperative circulatory and respiratory complications are presented and are discussed in detail.

University Hospitals, 1300 University Ave. (6) (Dr. Bamforth).

Factors Concerned in Incidence of Death in 2186 Cases of Pulmonary Resection

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The concluding paper in this study presents an analysis of patient mortality in our series of 2186 cases of pulmonary resection. For the purposes of this study mortality is defined to include all patients who were given an anesthetic for the performance of a pulmonary resection and who died during the postoperative period while still in the hospital. Patients who died during a subsequent admission, who died at home, or at another hospital, or whose disease was found to be inoperable and who, therefore, were not subjected to a pulmonary resection are not included in this study. No attempt is made to distinguish among the various groups of patients whose death may be attributed, only arbitrarily in many cases, to anesthetic complications, to surgical complications, or to unrelated causes. We wish again to emphasize that it is not our intention to compare the results of this study with any of the results published from other sources. Without knowing the exact circumstances of every anesthetic administration and all the details of surgical technique and care, such comparisons are necessarily on the most tenuous grounds, and are likely to be highly misleading. For this reason, the accompanying Tables are presented without references and with only explanatory notes.

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TABLE 1.—*Annual Incidence of Mortality Following 2186 Pulmonary Resections from 1941 to 1955, Inclusive*

	Deaths	Cases	Percentage
1941	3	11	27.3
1942	1	7	14.3
1943	3	5	60.0
1944	4	9	44.5
1945	0	33	0
1946	6	46	13.2
1947	4	85	4.7
1948	10	145	6.9
1949	9	130	6.9
1950	6	183	3.3
1951	13	270	4.8
1952	8	330	2.4
1943	8	387	2.1
1954	8	304	2.6
1955	4	241	1.7
Total	87	2186	3.98

The total number of patients who died after pulmonary resections is shown, by year, in Table 1. The distinct improvement in mortality from 16.9%, in the first five years of the study, to 2.7%, in the last five years, can be attributed to a number of factors. Increased surgical and anesthesiological experience, the more liberal use of whole blood, the introduction and use of more powerful antibiotics, and the introduction of new anesthetic agents and techniques have all contributed to this reduction in mortality.

TABLE 2.—*Age of Patients in Eighty-Seven Deaths Following 2186 Pulmonary Resections*

	Age, Yr.										
	Less than 1	1-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	Over 80	Total
Deaths	0	1	4	13	8	15	17	24	5	0	87
Total cases	3	42	147	515	505	436	311	194	31	2	2186
Percentage	0	2.4	2.7	2.5	1.6	3.4	5.5	12.4	16.1	0	3.98

TABLE 3.—*Mortality Following 2186 Pulmonary Resections: Distribution by Physical Status*

	Elective				Emergency			
	1 Good	2 Fair	3 Poor	4 Bad	5 Good	6 Poor	7 Moribund	Total
Deaths	0	28	52	7	0	0	0	87
Total cases	21	1376	762	21	1	3	2	2186
Percent	0	2.1	6.8	33.3	0	0	0	3.98

The incidence of death tabulated according to the patient's age is given in Table 2. The sharp increase in the incidence of death in patients above the age of 50 is quite impressive and is significantly higher than the postanesthetic mortality in the same age groups in patients who had operations other than pulmonary resections. It would appear from this comparison that the degenerative changes appearing in the older age groups may be of greater significance in the outcome of pulmonary resections than in most other types of surgical procedures.

TABLE 4.—*Duration of Anesthesia, in Minutes, in Deaths Following Pulmonary Resection in 2186 Cases*

	Duration, Min.							
	Less than 60	60–90	90–120	120–180	180–240	240–300	Over 300	Total
Deaths	0	4	12	29	24	13	5	87
Total cases	17	156	426	1032	412	104	39	2186
Percentage	0	2.6	2.8	2.9	5.8	12.5	12.9	3.98

The incidence of death tabulated on the basis of physical status is shown in Table 3. The observation that mortality increases markedly in Group 3 (poor status), and Group 4 (bad status) is not unexpected.

The incidence of death tabulated on the basis of the duration of anesthesia is presented in Table 4. It is apparent that the mortality rate increases in direct proportion to the duration of anesthesia. One of the causes for this increase is the fact that patients having the most extensive pathological findings, and thereby presenting the most difficult surgical problems, require a considerably longer time for the performance of pulmonary resection. It is our distinct impression, however, that, aside from this rather obvious fact, the marked increase in the postoperative mortality in cases of resections lasting longer than four hours may be due, perhaps, to the increased duration of anesthesia.

The incidence of death tabulated on the basis of the principal anesthetic agent used is presented in Table 5. The strikingly high mortality following cyclopropane anesthesia requires a word of explanation, and the findings as presented should probably not be accepted fully at face value. If the incidence of death by agent is analyzed on an annual basis, it is found that there is a distinct difference in the percentage distribution of mortality during the first 10 years of the study and that during the last five years. The over-all mortality rate following cyclopropane anesthesia from 1941 to 1950 was 16.5%, while from 1951 to 1955 the postcyclopropane mortality was only 3.9%. There was much less change in the mortality following ether anesthesia. With this agent the mortality from 1941 to 1950 was 5.4%, and from 1951 to 1955 it was 4.3%. No such comparison is possible for nitrous oxide, since this agent was not used in

TABLE 5.—*Agents Used in Eighty-Seven Deaths Following Pulmonary Resection*

	Chloroform	Cyclopropane	Ether	Nitrous Oxide	Others	Total
Deaths	0	23	49	15	0	87
Total cases	17	232	1005	900	32	2186
Percentage	0	10.0	4.8	1.6	0	3.98

this series before 1949. It seems likely that the factors responsible for the very high mortality in the early years of the study must include a relative lack of surgical and anesthesiological experience, a less liberal use of whole blood, and the absence of antibiotics from the surgical armamentarium. These considerations modify the interpretation of the over-all statistics and tend to exonerate cyclopropane to a certain extent. They are not sufficient, however, to explain completely the fact that during the last five years of the study the mortality following cyclopropane anesthesia was 3.9%, following ether anesthesia it was 4.3%, and following nitrous oxide-thiobarbiturate-curare anesthesia it was only 1.7%.

TABLE 6.—*Use of Muscle Relaxants in Eighty-Seven Deaths Following 2186 Pulmonary Resections*

	Curare	No Curare	Total
Deaths	29	58	87
Total	1218	968	2186
Percentage	2.35	6.0	3.98

The incidence of death tabulated according to whether or not the patient had received a muscle-relaxant agent during anesthesia is indicated in Table 6. Some of the observations made in the preceding paragraph pertain also to this Table, and it has to be remembered that curare was not used widely in clinical anesthesiology until about 1949. It may be incorrect to claim that the introduction of curare into anesthesia for thoracic surgery significantly decreased operative and postoperative mortality. It is quite obvious, however, that it has not raised the incidence of death and that the findings in the curare group compare most favorably with the findings among the patients who have not received a muscle-relaxant agent.

The time of death and the cause of death in this group of patients are shown in Tables 7 and 8. Of these, 13 patients died in the operating room, and another 13 died during the first 24 hours postoperatively.

TABLE 7.—*Time of Death in Eighty-Seven Deaths Following Pulmonary Resection*

	In Operating Room	24 Hr. Postoperatively	Later	Total
Circulatory	8	8	26	42
Respiratory	5	5	31	41
Central nervous system	0	0	3	3
Other	0	0	1	1
Total	13	13	61	87

In each of these two groups, eight patients died of circulatory complications, and five patients died because of respiratory difficulties. Among the patients who died more than 24 hours postoperatively, 26 deaths occurred from circulatory and 31 from respiratory causes. Only four patients in the entire group died of other complications.

Summary

The incidence of 87 deaths in a series of 2186 cases of pulmonary resection is analyzed on the basis of annual distribution, age, physical status, principal anesthetic agent used, duration of anesthesia, use of curare, and the time and cause of death. The study indicates that advanced age, poor physical status, and the increased duration

TABLE 8.—*Causes of Death in 2186 Cases of Pulmonary Resection*

Circulatory	
Pulmonary embolus	11
Circulatory failure	12
Myocardial degeneration	1
Coronary occlusion	1
Pericarditis	1
Severe hemorrhage (during operation)	6
Postoperative hemorrhage	9
Caval thrombosis	1
	42
Respiratory	
Empyema	3
Bronchopneumonia	5
Lobar pneumonia	1
Tuberculous pneumonia	6
Spread of tuberculosis	3
Aspiration	1
Atelectasis	6
Pneumothorax	2
Other mechanical disturbances	1
Anoxia, asphyxia	13
	41
Central nervous system	
Cerebrovascular accident	2
Cerebral abscess	1
	3
Others	
Paralytic ileus	1
Total	87

of anesthesia all increase the incidence of death. Cyclopropane and ether anesthesias were followed by higher mortality than was nitrous oxide-thiobarbiturate-curare anesthesia. One-third of the deaths occurred in the operating room or within 24 hours postoperatively. Respiratory complications caused the death of 41 patients. Forty-two patients died of circulatory complications. Central nervous system and gastrointestinal complications were responsible for the death of four patients.

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Aortic "Saddle" Embolism

Review and Report of Three Cases, One Twice Recurrent

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Although available methods have improved the results of treatment of aortic bifurcation embolism, only 64 successful operative results could be found in the English literature. No doubt many are unreported. Five recent successful aortic embolectomies in three patients, combined with improving embolectomy results in other vessels, encourage continued efforts to salvage limbs and life in such patients.

Previous Reports

In 1911 Labey reported the first successful arterial embolectomy, and Bauer did the first successful aortic embolectomy in 1913. McClure and Harkins,[35] in 1943, in a comprehensive review, surveyed the 690 reported arterial embolectomies and found 21 successes at the aortic level.

In 1950 Albright and Leonard [1] reviewed 193 recorded aortic embolisms and found 8 patients surviving conservative treatment and 26 living after embolectomy. They added a successful case. The same year the *Lancet* noted editorially [17] that over three-quarters of the approximately 200 reported patients had died and emphasized the need for reports of all successes as well as failures in order that future therapy may be guided by past experience.

In 1951 Taylor [56] surveyed the 27 reported successful aortic embolectomies and commented on the gloomy outlook of patients undergoing such an operation because of repeated embolism or fatal heart disease, since 12 of the 27 patients were known to be dead after three years.

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The year 1952 saw the reviews of Pool and Farrar [43] and Thiessen and Marxen,[57] who listed 32 and 34 reported successes, respectively, and added a single successful case each.

The advent of mitral commissurotomy for mitral stenosis resulted in a new proximate cause of embolism; and Bloomberg, Blumberg, and Haimovici [7] reported the first successful aortic embolectomy after mitral valvulotomy in 1952, removing the embolus four hours after the cardiac manipulation. Later cases have been reported since,[24,38,58,62] and in 1956 Denman and Hanson [15] recorded what they considered to be the 44th successful aortic embolectomy and the 8th successful postcommissurotomy.

Further case reports have slowly accumulated, and we found 21 patients reported to have survived aortic embolectomy beyond two weeks who have not been listed previously by the reviewers mentioned,[2,13,18,23,25,28,30,34,37,38,44,49,50,53,54,59,63,64,66] for a total of 64 successful aortic embolectomies.* These reports were surveyed not for any careful determination of total number but in order to summarize current knowledge of the causes, diagnosis, and proper treatment of this highly lethal lesion.

Origin of the Embolus

The embolus usually arises either from thrombosis within a rheumatic heart with mitral stenosis to which atrial fibrillation or operative trauma has been added, or from a mural thrombosis secondary to myocardial

*This figure is minimal, since only English-language national journals were reviewed and some cases were no doubt overlooked. The figure serves to indicate that successful operative results are increasing but are still not many.

Sources of Aortic Embolism

1. Rheumatic heart disease with mitral stenosis
   (*a*) Recent rhythm change
   (*b*) Recent operative trauma
2. Intracardiac mural thrombosis
   (*a*) Infarction
   (*b*) Trichinosis
3. Atrial fibrillation due to hyperthyroidism, arteriosclerosis, or other heart disease
4. Valve vegetation due to endocarditis
5. Aortic disease
   (*a*) Atherosclerotic plaque
   (*b*) Aneurysm
   (*c*) Syphilitic aortitis
6. "Paradoxic embolus" via septal defect
7. Intracardiac tumor

infarction (Table). Rare causes include myocardial trichinosis,[65] atrial fibrillation due to other forms of heart disease, and valvular vegetations due to endocarditis. Atherosclerotic plaque, aneurysm with thrombosis, and syphilitic aortitis[46] may allow release of emboli from thrombosis of the aortic wall. Learmonth[31] thought that paradoxic embolism (venous embolism passing through an atrial or a ventricular septal defect[6]) particularly occurred in children and also warned that "pseudo-embolism" of the aortic bifurcation might be due to iliac embolism or to severe arteriospasm secondary to lodging of a small embolus close to the aorta. Rothstein[48] discussed particularly the cases of aortic embolism and thrombosis which have been found in infants, and the rarer causes of these.

The Clinical Syndrome

The classical evidence of saddle embolism is sudden bilateral lower-extremity vascular insufficiency, denoted by pain, pallor, sensory and motor losses, and absence of pulses, to which may be added abdominal, low-back, buttock, or perineal pain or paresthesia, depending upon the adequacy of circulation via collaterals. It should be clearly understood, however, that the "classic" signs of this, as well as many other diseases, are actually late signs and that the symptoms and signs in the early phase are less striking and more demanding of diagnostic ability. Jepson's[27] description of the clinical course of peripheral embolism is excellent and stresses the common onset of symptoms by distal paresthesias. Some of the cases reported herein occurred during the course of hospitalization and allowed a clear understanding of how easily overlooked may be the early evidences of saddle embolism. Lack of pain is apt to be misleading. The occurrence of this during the early postanesthetic period following mitral commissurotomy has led to the present policy of hourly pulse examinations by the nurse or attendant to prevent overlooking such an embolism for long periods when the patient himself does not complain. However, it has been noted previously that there may be a femoral pulse transmitted through the embolus (Nordentoft's sign). Burt, Learmonth, and Richards[10] found this to be true in four of their seven patients examined within six hours of onset, although none had a pulse distal to the femoral artery. Our second case showed this phenomenon.

It should be emphasized that, since aortic embolism is considerably better treated early than late, there should be a change from diagnosis on the basis of late findings to diagnosis from early or minimal history and findings. Pulse and oscillometric examinations ordinarily should allow quick determination of the situation. Kolff[30] reported the aortographic diagnosis of a single case in 1955 but noted that the prolonged postoperative anuria necessitating artificial kidney dialysis seemed likely related to that aortography. It is doubtful that such examination will be often warranted in view of the increasingly acknowledged risk of aortic injection of hypertonic iodinated compounds. Aortography in the later phase, in which collateral circulation is maintaining viability, may be necessary to clarify operative indications, as discussed by Olwin, Dye, and Julian.[41]

In general, leg paresthesia, coldness, or pain should alert one to the possibility of arterial embolism, particularly when associated with known heart disease and either atrial fibrillation or a recent myocardial infarction. Immediate examination rules out

bifurcation embolism if there is any pulse distal to the femoral on either side. Presence of a femoral pulse does not necessarily mean there is not an aortic embolus. Oscillometric study confirms palpation findings.

Indications for Operation

The outlook for both life and limb is poor without embolectomy. Although Walker [61] did report survival after saddle embolism (with later loss of a leg) and commented on other non-autopsy-proved survivals, general experience indicates a high death or amputation incidence among nonoperative cases.

Reich,[46] in 1943, reported that only one of seven patients not operated on survived. Andrus [2] found that 6 of 10 saddle emboli occurred so late in the course of heart disease as to make any treatment ineffective. One survivor and one patient who died had embolectomy. He concluded that should be done if the general status permitted. Jepson [27] reported that four of seven limbs were lost following nonoperative treatment of aortic embolus and therefore advised early operation. Burt, Learmonth, and Richards,[10] in 1952, reported 16 cases of aortic embolism. Only two of eight patients treated conservatively lived without loss of leg. Four of eight were operated upon successfully.

Schein, Hoffert, and Hurwitt,[49] in 1956, discussed 11 consecutive saddle emboli operated upon by eight different surgeons. Of the 11 patients, 3 survived, while 4 died of cardiac arrest and another just as operation began. The authors believe that abdominal and back pain indicate a poor prognosis because of proximal thrombosis. Poor outlook was also associated with delay in operation and arteriosclerotic rather than rheumatic heart disease. They advocated nonoperative treatment if over eight hours had elapsed, because of almost certain operative failure. We do not agree with this time contraindication to operation, because of the known great risk if the acute aortic block persists and because in certain cases longer-delayed operations have been successful and more success can be expected with increasing vascular surgical experience.

Successes after more than 8 hours' delay have been reported by Taylor [56] (in 2 of the collected cases the delay was 6 hours); by Massell [38] (a delay of 16 hours); by Ewing [18] (a delay of 24 hours); by Pratt [44] (a delay of 60 hours); by Warren, Linton, and Scannell [62] (a delay of 13 hours), and by Olwin, Dye, and Julian [41] (restoration in 4 of 6 peripheral embolectomies done 22 hours to 3½ months after occurrence). Some of these more delayed cases probably had viability due to sufficient collateral blood flow and operation was a thrombectomy rather than an embolectomy.

While four of our aortic emboli were operated upon with less than eight hours' delay, we would not hesitate to attack an embolus with longer delay if the general situation permitted, as in Case 2 (nine-hour delay). At least a transfemoral retrograde approach could probably be tolerated by any patient if the transabdominal route were judged too risky. In the third embolectomy in our Case 2 this method was used.

Veal and Dugan,[60] in 1951, advised immediate procaine sympathetic block for arterial embolism and stated the belief that if circulation did not return at once operation should be performed. We agree with this in theory because an occasional patient has definitely improved after procaine block for peripheral embolism and has not required operation. However, in practice this policy is almost certain to delay embolectomy needlessly because of time requirements in obtaining block materials and because few surgeons can make an operating-room team and its equipment stand by during such a test, and may not be able to operate promptly if the test fails.

In both Case 1 and Case 2 we used block, without results. In Case 3 the operating room was called at once and no block was attempted. If procaine block is to be used, it must not be allowed to add hours to the delay time.

Report of Cases

The following three cases actually represent five aortic bifurcation embolisms, since the second case was unique in having three distinct and separate saddle emboli removed surgically.

CASE 1.—On Sept. 15, 1953, a 36-year-old white woman had a mitral commissurotomy for mitral stenosis. When the left atrial appendage was opened, adherent clot was observed within. This was removed by flushing and by actually excising parts of it which were firmly attached to the wall. The valve was fractured with the finger while intermittent external-carotid-artery pressure was made. Operation was completed at 11:10 a. m.

In the early recovery period the patient began to complain of numbness in the left leg, and by 1:00 p. m. there was coolness of both legs below the midthigh with absence of sensation below the knee on the left side. All muscle motions were good. A left paravertebral block was done with 1% procaine hydrochloride, without change in signs. At 4:00 p. m. the left femoral artery was explored under local anesthesia. It was found to be diminished in size and did not bleed when opened. A large ureteral catheter was passed up toward the aorta without removing any clot. The wound was loosely packed while general anesthesia was induced with ether. A midline incision was made in the abdomen. The bifurcation of the aorta was exposed and a firm mass palpated at this point. There were no pulsations in either iliac artery. A curved Crafoord clamp was placed on the proximal aorta, and Penrose drains were pulled up about the iliac arteries distally. A longitudinal incision was made over the aorta just proximal to the bifurcation and a well-formed saddle embolus immediately popped out. When the aorta was flushed by temporarily loosening the proximal clamp, another chunk of embolus popped out. After embolectomy the common iliac arteries had good pulsations but were decreased in size. This was not changed by the intra-arterial injection of 50 cc. of 0.1% procaine hydrochloride. After 30 minutes pulsations could be felt in the proximal left femoral artery through the thigh wound, which was still open; so this arteriotomy was closed. A left lumbar sympathectomy was performed, and the patient was returned to the floor in good condition.

Two hours later no pulses could be felt in either leg, but they were warm. Two days after operation, both legs were warm, and all pulses were palpable on the right, although none could be felt on the left. A month later the patient noted some fatigue on walking, particularly in the left leg, but had no other symptoms.

In July, 1954, the patient was readmitted for several days because of upper anterior chest pain, radiating to both arms, associated with severe headache. Examination and films revealed infiltration in the left lower lung field, which was finally thought to represent virus pneumonitis, although the question of pulmonary embolism was considered. The infiltration cleared rapidly, and she was not seen again until Oct. 11, 1954, at which time she returned complaining of a drawing pain in the right thigh. There were no definite signs of peripheral arterial embolism, although, because of the history, the patient was brought into the hospital for anticoagulant treatment for two days, and this was maintained on the outside after her discharge. While she was in the hospital, there was a brief episode of upper abdominal pain without signs. This raised the question of mesenteric embolism.

In March, 1955, she was briefly hospitalized for excision of ingrown toenails under nerve-block anesthesia.

In December, 1956, she was hospitalized for study of hypertension and controlled by drug therapy. No left-leg pulses were felt, but the left leg was asymptomatic three and one-quarter years after embolectomy.

Comment.—There was no preoperative history indicating embolism. However, the thrombus found at cardiotomy immediately raised the possibility of such at operation. Upon the patient's return to her room, the special nurse noted pallor and coldness of the left leg. Examination now showed complete absence of pulses, although the right lower extremity and left thigh were warm and pink. Paravertebral block failed to change the signs; so left-femoral exploration was done first, in an atempt to avoid laparotomy. Failure by that route led to immediate and successful direct aortic embolectomy, which was well tolerated by the patient. It was at once apparent that the left iliofemoral arterial tree was quite spastic, although pulsation did return as far down as the proximal femoral artery. Lumbar sympathectomy failed to change this. No pulses ever returned to the left extremity, although there are good nutrition and exercise tolerance. It is assumed that either embolism or surgery led to thrombosis in the iliac artery on that side.

The further history of this woman probably indicates recurrent smaller episodes

of embolism, although another operation has not been necessary. Fifteen months have now elapsed since the last episode. After considerable discussion, she is being treated with small biweekly doses of bishydroxycourmarin (Dicumarol) in an effort to prevent further thromboembolism.

CASE 2.—A 49-year-old woman was admitted on Jan. 31, 1955, following sudden lower abdominal discomfort going on to severe pain, with a "restless feeling in both legs." The previous history showed that she had been under a physician's care for mitral stenosis since 1928, without decompensation or physical inactivation at any time. She had never had atrial fibrillation.

Twelve days before admission she developed a cold and began to take prophylactic penicillin by mouth, as previously instructed. Two days before admission her husband found her lying partially out of bed and quite weak and pale. She was found to have atrial fibrillation and was immediately treated with quinidine. Eighteen hours later the cardiac rate was regular, at 76 per minute. All leg pulses were palpable at that time. On the day of admission she developed numbness of both legs at 1:00 p. m. Her physician was called and saw her five hours after onset. Her heart was found to be regular. There were no pulses in either lower extremity.

First Aortic Embolectomy.—On the diagnosis of saddle embolism of the aortic bifurcation, operation was started, nine hours after onset of symptoms. The peritoneal cavity was opened through a left paramedian rectus-splitting incision. There was a good pulsation in the aorta to within 3 cm. of the bifurcation, where the pulses abruptly stopped and where a mass could be palpated within the aorta. The iliac arteries were occluded by rubber drains and the proximal aorta by an unlocked Satinsky clamp. A 2 cm. longitudinal incision was made just proximal to the bifurcation of the aorta and an organized blood clot removed. This had the configuration of the aorta, with two short iliac extensions. The iliac vessels were allowed to bleed and good flow obtained. Upon temporary release of the clamp on the proximal aorta several small clots were flushed out from above. The clamp was reapplied and the aorta closed with a continuous 00000 nonabsorbable surgical (silk) suture placed as a running over-and-over suture.

At conclusion of the operation the femoral pulses were palpable, and after one hour the popliteal arteries were definitely palpable. Atrial fibrillation recurred two days later. This was treated with quinidine. Ethyl biscoumacetate (Tromexan) was also started. The next day, the dorsalis pedis pulses became palpable, and so the previously placed epidural catheter, for instillation of lidocaine (Xylocaine), was removed. Atrial fibrillation continued despite use of quinidine, and the patient was discharged with the irregularity on the 23d postoperative day. She was maintained on ethyl biscoumacetate.

She was next seen in the emergency room seven months later, on Sept. 5, complaining of pain in both legs and numbness of the feet. The history showed that a month previously, while in another city, she had had a similar pain upon arising and leaving a movie. She had hardly been able to walk and had been carried to a hotel in a taxi. The pain in the back and thighs and weakness of the legs continued for about 48 hours but gradually subsided without any treatment. This episode followed cessation of anticoagulant therapy at the time that she left on vacation. The present episode had started one hour and a half before the patient was examined. There was a pulsation in the proximal aorta but no pulses distal to this. The feet were cold, and the capillary return was delayed. The oscillometer failed to show pulsation at any point in the legs. The diagnosis of recurrent aortic embolism was made.

Second Aortic Embolectomy.—Four hours after onset the patient was operated upon through the previous left paramedian incision. This time the left rectus muscle was retracted laterally. There were extensive adhesions over the bifurcation of the aorta; so the lateral attachment of the descending colon was severed, the descending and sigmoid colon reflected medially, and the aorta approached from the retroperitoneal position. The left ureter was identified and preserved, as was the inferior mesenteric artery. The aorta had pulsations down to an area of perivascular scarring, below which no pulsations could be felt. The fibrotic tissue over the bifurcation of the aorta was carefully dissected and the previous suture line exposed. The silk suture was cut at several places and pulled out of the aortic wall without perceptible damage. A Satinsky clamp was applied proximally and rubber drains distally. The previous aortic incision was reopened, and a clot, quite similar to the one previously removed, was taken out. Free back-bleeding was obtained from the iliac vessels. The proximal clamp was loosened and the vessel flushed. The aorta was closed with a continuous 00000 silk suture. Both common iliac arteries now pulsated well. It was noted that the right common iliac artery was the site of an almost completely circumferential area of calcification, which was segmental and which was 2 to 3 cm. long. The abdomen was closed in layers, and mattress stay sutures were pulled up to bolster this. Immediately after operation a continuous epidural block was started. The patient was out of bed on

the first postoperative day and gained strength rapidly after this operation. At the time of discharge all pulses were palpable on the right side but none on the left. She was discharged on the 12th postoperative day on prophylactic bishydroxycoumarin treatment, since she had previously become refractory to ethyl biscoumacetate. On the 25th postoperative day she was examined in the office, at which time the wound was healing well. All pulses were now palpable except the left dorsalis pedis and the left popliteal. She was advised to undergo left atrial appendectomy and mitral commissurotomy.

Mitral Commissurotomy.—She reentered the hospital on Oct. 13, 1955 (the 39th postoperative day), with continued atrial fibrillation. On Oct. 15 mitral commissurotomy and amputation of the atrial appendage were performed through a left lateral thoracotomy. There was an extremely large atrial appendage, with many finger-like projections. It was thought that this would lend itself to the formation of mural thrombi. However, on palpation no definite thrombus could be felt. The finger was inserted into the atrial cavity and a moderate degree of mitral stenosis ascertained. The anterior commissure was fractured. There was a small amount of calcification in the posterior commissure. This was partially divided until the opening was estimated to accommodate two fingers. At no time was any thrombus encountered. The patient's condition was good, and operation was finished at 10:50 a. m. At noon the patient was still hypotensive, but both femoral arteries were palpable. The blood pressure gradually increased.

At approximately 6 p. m. the right foot was noted to be pale and cool. The oscillometer failed to show oscillations in either thigh or calf. Motor and sensory functions were normal. The only pulse palpable was the left femoral. The oscillometer showed a flicker in the left thigh and a barely perceptible flicker in the right thigh. There were no pulsations in the calves. A diagnosis of recurrent postoperative embolus was made, but, because of the pulsation in the left femoral artery, there was doubt as to whether it was lodged at the aortic area or whether it had slipped into the right iliac bifurcation. The patient was observed following an epidural procaine block, at which time there was no change in pulsations or oscillometric findings.

Third Aortic Embolectomy.—Accordingly, at 12:20 a. m., the right femoral artery was explored under 1% procaine hydrochloride anesthesia. When the common femoral artery was opened, there was moderate back-bleeding from the distal superficial femoral and deep femoral arteries, but no bleeding from the proximal common femoral artery. A very large polyethylene catheter was selected to fit the common femoral artery proximally. This was pushed up beneath the inguinal ligament to a level measured to be at the umbilicus before any clot was obtained. At this time definite clot was sucked back with a syringe. About 30 minutes was spent in removing this clot and about 250 cc. of blood. At this time there was free flow of blood from the proximal femoral artery, but it was without pulsation; so it was thought that there was still obstruction at the aortic bifurcation level. There was difficulty with cessation of the transfusion for mechanical reasons at this point, and the patient's condition became extremely poor. Operating was stopped while a new intravenous needle was placed at a different site. Because of the patient's poor condition, it was decided to close the femoral arteriotomy with a nonpulsatile flow of blood, hoping that would save the leg. However, just prior to closure, a final attempt was made to pass the polyethylene catheter, and a slightly smaller size was selected. This was pushed up to the level of the umbilicus and a definite clot removed, after which the catheter passed freely well up into the proximal aorta. Upon removal of the catheter, there was a strong pulsatile flow of blood. The femoral artery was, therefore, quickly closed with a continuous 00000 silk suture and the operation terminated by a continuous silk suture in the skin of the thigh. At conclusion of the operation the left femoral pulse was strong, but no other leg pulses could be felt.

On the first postoperative day, the vital signs were stabilized. The legs were still warm, but both feet were quite cool. Only the left femoral pulse was palpable. At the time of hospital discharge, 20 days after operation, both femoral pulses were palpable. The left dorsalis pedis could be felt, but not the right. Skin color and temperature were bilaterally good and equal.

After 18 months there has been no further difficulty. She walks well and has no claudication, despite absence of lower-leg pulses, as noted. Oscillometry shows only a flicker in the right calf and none in the left. Nevertheless, color is well maintained with legs elevated. Capillary return is slow in this position. Both feet are warm.

Anticoagulant therapy was maintained for eight months.

Comment.—The initial aortic embolism was clearly related to conversion of atrial fibrillation 13 days before. After successful aortic embolectomy, the question of mitral valvulotomy was considered, but the procedure was not carried out, chiefly because the patient had never had any real cardiac symptoms.

Six months later, the symptoms of leg pain and numbness while the patient was

in another city strongly suggested recurrent embolism. However, without treatment this cleared over a 48-hour period. The resolution of symptoms, therefore, suggested a small embolus with accompanying vasospasm. Knowledge of this history caused concern regarding diagnosis when the patient presented in the emergency room with the second aortic embolism. The history and signs appeared clearly to indicate recurrent saddle embolism at the aortic bifurcation; yet by history a similar syndrome had spontaneously ended a month before. After some consideration a nonoperative course appeared unduly risky, and operation clearly showed a large, blocking saddle embolus.

At the second direct aortic embolectomy, the final approach was retroperitoneal, by reflecting the descending colon. This made dissection of bowel adhesions unnecessary and afforded good exposure without difficulty. The aorta did not appear at all narrowed at the site of previous arteriotomy and, in fact, was in such good condition that the previous suture was simply picked out to allow the aorta to be reopened at the same site.

Mitral commissurotomy was now definitely advised in order to decrease likelihood of further embolisms. At operation no clot was found within the atrium. Immediately afterward, both femoral vessels were felt. The discovery of a cool and pale right foot seven hours after operation again suggested embolism, particularly since the previously palpable right femoral pulse had disappeared. Large-bore polyethylene catheter exploration of the artery did not completely clear the vessel until (by external measurement) the catheter passed proximal to the aorta bifurcation. It is possible that thrombus building up proximal to the embolus accounted for this, or the catheter may have pushed the clot more proximally as it passed. In any event, this technique allowed the arterial passage to be cleared without resort to a third transabdominal arteriotomy.

She was maintained on bishydroxycoumarin for eight months after operation. When last examined, on March 1, 1957, she had been off that drug for 10 months, without difficulty. Eighteen months after the last embolectomy she walked well and showed 2 units of oscillation at each calf.

Successful repeated multiple peripheral embolectomy is well known. Pearse,[42] in 1933, reported such a case in reviewing 296 reported embolectomies. Strömbeck,[55] in 1935, stated that 5 of 327 Swedish embolectomies were multiple. Other cases [14, 19,35,36,47,50,51,59,62,64,66] have been reported, an unusual case being that of Fiddian,[19] who described simultaneous arm embolism. A right axillary embolectomy was done under brachial-plexus block; "the patient was given a cup of tea and a cigarette," and a half-hour later an embolectomy was done on the left brachial artery!

Several cases of successful aortic plus peripheral embolectomy have been reported,[25,45,66] and at least one repeated aortic embolectomy (embolectomy by Nyström, in 1929, followed by a second one, by Westerborn, in 1931 [55]). Our case exceeds this number by one.

Case 3.—A 71-year-old white woman was hospitalized on May 10, 1956, for pulmonary edema. The history indicated a probable myocardial infarction 18 years previously and intermittent digitalis medication since that time. In recent years, hypertension had been present, and she had been given drug therapy for this. For six months there had been intermittent dyspnea with episodes of nausea and vomiting, possibly related to digitalis toxicity. On the evening of admission, she suddenly became dyspneic, with substernal pain, and was admitted for treatment.

Physical examination showed an acutely ill white woman. The important findings consisted of cardiomegaly and slow atrial fibrillation. The femoral pulses were both palpable. She responded well to morphine, pressure oxygen, and rotating tourniquets. The following morning she vomited, but this did not recur.

On the fourth hospital day (May 14, 1956), about 4 a. m., there was severe pain in both legs with immediate coldness and inability to move the left leg. Both legs were cadaveric up to the knees (Fig. 1) and without sensation distally. There were no pulses distal to the aortic bifurcation, although

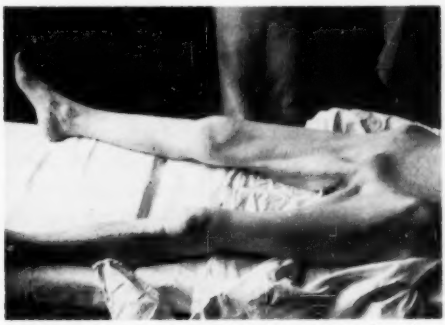

Fig. 1 (Case 3).—Cadaveric legs of patient just prior to laparotomy.

Fig. 2.—Operative exposure of aortic bifurcation with embolus bulging through incision. Penrose drains lie around common iliac arteries. Tip of aortic occluding clamp is seen at right.

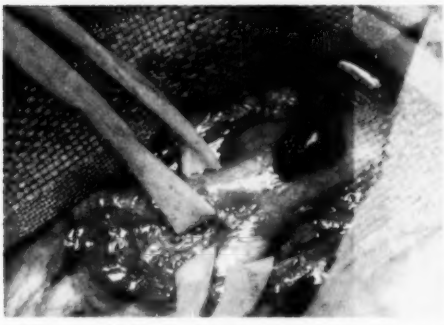

Fig. 3.—Embolus almost completely extruded from aorta.

Fig. 4.—Aortic "saddle" embolus and iliac "tails" after removal.

Fig. 5.—Polyethylene catheter suction to iliac artery through aortic arteriotomy (at right by sucker tip). Central clamp points to dark clot in suction catheter.

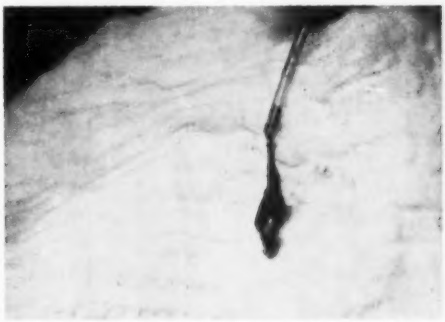

Fig. 6.—Dark, soft, formed embolus in tip of polyethylene catheter just after its removal from iliac artery.

a proximal aortic pulsation was palpable. Operation was performed seven and one-half hours after the initial complaint, under ether and cyclopropane anesthesia. Folliwing isolation of the aorta and common iliac arteries, a Satinsky clamp was partially closed on the proximal aorta, and this vessel was opened for 15 mm. proximal to the bifurcation (Figs. 2 and 3). A dark, soft, but formed thrombus extruded (Fig. 4). Proximal aortic flushing was performed. There was no backflow of blood from the iliac arteries. A large polyethylene catheter was threaded down each of these into the distal thigh region and many dark clots sucked back until there was excellent retrograde

blood flow (Figs. 5 and 6). The aortic wound was closed with a continuous 00000 silk suture and the operation terminated. At conclusion, the patient's condition was good; and both femoral arteries were pulsating strongly, although more distal pulses could not be felt. The left popliteal pulse became palpable four hours after conclusion of operation, and the next morning the right popliteal pulsation was palpable. Color, sensation, and motor power returned, and the patient was able to walk, although she was feeble. On the 12th postoperative day the patient complained of pain in the left thigh, and the pulses on the left distal to the femoral became absent. The left foot was slightly cooler, and a diagnosis of small popliteal embolism was made. The motor and sensory function of the left leg, however, continued to be good. On the 21st postoperative day there was left anterior chest pain for about one hour without change in the physical signs. A new EKG showed no particular change, but, in fact, improvement in the S-T segment over the previous tracing eight days before. The patient was discharged on June 8, 1956 on digitalization, with continued atrial fibrillation, but with a well-healed wound and able to walk very satisfactorily.

Ten months after operation she is alive and well and walks without difficulty. No further embolization has occurred.

Comment.—This is the third surgically treated survivor of aortic embolism. Her diagnosis was quite apparent, and operation was uneventful. Some minor postoperative emboli did not require surgery. Despite her age and cardiac status, she has returned to her preoperative level of activity.

General Comment

Operative Technique.—We prefer the direct transabdominal approach to the aorta, bearing in mind that the aortic bifurcation is at the level of the umbilicus and that the approach should be through an incision centered on the navel, rather than a low abdominal incision. The exposure must be long enough to allow the viscera to be packed away and to allow both proximal and distal vascular control. We prefer either a longitudinal left paramedian incision, with retraction of the rectus muscle, or a midline incision.

Ordinarily, one should initially aim for proximal control of a large vessel, such as the aorta. Aften opening the posterior peritoneum and overlying areolar tissue and fascia, the surgical plane of the aorta is entered, allowing relatively bloodless dissection. The vena cava, on the right, and the short lumbar arteries, posteriorly, must be avoided as the aorta is encircled proximal to its bifurcation. Several methods of proximal control are possible, but we find it easy to pass a Satinsky or Harkens clamp for proximal occlusion. This is never closed and locked but is held constantly by one member of the team, who closes it just enough to stop blood flow but not to damage the aortic wall.

Distal iliac control is similarly gained by opening the posterior peritoneum and fascia and passing a Penrose drain about the artery, carefully avoiding the iliac veins. A Penrose drain may then be easily used to control backflow from the iliac vessels.

While some suregons have advocated iliac arteriotomy, we prefer to make a longitudinal opening in the distal aorta in order to remove the clot. There need be no fear of making this incision long enough for proper working room. Placement of complicated suture arrangements is unnecessary and unwise because of likely damage to the lips of the wound. However, it is often helpful to place a single 00000 silk suture through each lateral edge of the wound, place light clamps on the ends of these stay sutures, and use them to hold open the arteriotomy, rather than handle the edges with forceps.

After popping out of the main embolus, the proximal clamp is loosened to permit flushing from above. The distal iliac vessels should now be opened, in turn, to be certain there is good backflow from each. Failure of such backflow indicates nonpatency of the distal arterial system, and steps should be taken to clear these vessels. This procedure is discussed below.

Aortic closure may be simply done by a continuous over-and-over suture of 00000 silk tied at one end, run up to the other, and brought back over itself and tied again at the original end. This is our standard

arteriotomy closure and has always proved satisfactory. (More complicated techniques are probably just as good.) Inspection of the healed suture line at the second aortotomy in Case 2 showed the excellent healing which follows this closure.

Standard abdominal closure completes the operation. The posterior peritoneum over the aorta does not require closure, although it may be tacked with a few interrupted sutures.

Particular circumstances may require deviation from the plan above. In the face of peritonitis or of adhesions (as in the second laparotomy, Case 2), it may be better to make a retroperitoneal approach from the left. Taylor [56] discusses and pictures this well. We have used it for aortic-node dissection but not for embolectomy, because the contralateral iliac seems poorly exposed.

The retrograde femoral approach to the aortic embolus possesses the disadvantages of a blind, indirect method, yet may allow success with a local anesthesia and thereby avoid laparotomy. Blum reported six aortic embolectomies, with a single survivor, in 1955 and believed that both femoral arteries should initially be explored and clamped with soft clamps to prevent distal passage of emboli during the aortic embolectomy.[8] This method was tried twice in this series, both times in the early recovery phase after mitral commissurotomy. It failed once and succeeded once, but deserves a place as a procedure of second choice. The use of large polyethylene catheters to go after the proximal clot is much better than the ureteral catheters and rubber tubes, used previously. These are kept continuously available in graded sizes of 30 in. tubings, each with its own adapter for a 50 cc. syringe.

Arteriospasm After Embolectomy.—Ordinarily, after the lumen of the vessel is cleared and the blood flow established, spasm in that vessel is no longer a problem, although distal vascular spasm may be postulated. We believe that many cases of such spasm are instances of distal thrombosis and that this should be cleared, as described below. Occasionally we have observed spasm in a femoral vessel under direct observation, although not in the aorta. Despite theories which have grown into statements as of fact, there is poor understanding of why vascular spasm occurs at times but not at others. We have observed definite spasm in the femoral or smaller vessels but not in the aorta. Papaverine applied locally may not successfully relieve it, and it may also prove refractory to local adventitial infiltration with procaine, adventitial removal, and intra-arterial procaine. This refractoriness occurred in the first case in which persistent femoral arterial spasm occurred.

Kinmonth and associates [29] have reported the production of arterial spasm in monkeys and relief by local application of 2.5% procaine hydrochloride. However, he noted that spasm could not be uniformly produced by rubbing or stretching monkey arteries, and the same has been found here in dogs.[12] We currently think that the most reliable relief of spasm occurs after a good blood flow is resumed and some time elapses, and that thereapeutic agents are apt to be of little value.

Proof of Patency of Distal Vessels.—Thrombosis of the distal vessels occurs at a variable, but ordinarily brief, time after embolism occludes the main circulation. Reestablishment of the arterial supply to the extremities depends upon distal vascular patency, just as it does upon removal of the aortic block. The course of the symptoms and signs in some patients even suggests that the distal thrombosis of vessels, rather than the main aortic occlusion itself, may cause the critical loss of arterial supply. The reported survival of patients (and their limbs) without operation undoubtedly depends upon collateral vessels carrying sufficient blood to patent distal vessels to maintain viability. Considerable care should be taken to ensure that the distal vessels are still patent or that they are opened up at operation. The efforts may be consid-

erably more involved than the aortic embolectomy itself.

Release of the operative occlusion of the common iliac arteries may allow a fairly brisk but nonpulsatile backflow of blood to appear, indicating iliac filling via collateral vessels. This flow may, of course, occur in the presence of thrombosis at a distance below the opening in the iliac vessel. In our third case there was moderate backbleeding from the right iliac artery, although subsequent catheterization removed a long thrombus from the femoral region. It, therefore, seems advisable to prove positively distal vascular patency by catheterization prior to closure of the aortic incision. Previous reports of arterial catheterization techniques have been made.[51] We have used long (30 in.) polyethylene tubes which are easily threaded down the iliac artery through the aortic incision. During passage of such a tube, negative pressure is maintained upon a syringe attached to it, to suck into its lumen any clot lying in the vessel. If resistance is encountered or free flow of blood into the syringe does not occur, the tube is removed for clearing of clot from it after it is advanced 1 or 2 in. Resistance also may indicate the tube to be too large for the artery as it passes distally, so that progressively smaller tubes are substituted. As clot is removed, the cleared arterial lumen is flushed gently with heparinized saline (50 mg. per liter). Such polyethylene tubes may be passed from aorta to popliteal artery if smaller ones are used distally.

Crawford and De Bakey[11] and Shaw[52] have recently reported their quite successful use of the retrograde saline-flush technique for the same purpose. In reviewing previous experience[36,41] with the catheter or cannula method detailed above, it is suggested that intimal damage, and later thrombosis, may result from such catheterization and that the retrograde flush technique is better. We do not doubt that such may occur and change the tube size as distal threading progresses in an effort to prevent this. Our experience with the catheter suction technique to date has been satisfactory, and it is certainly simple to perform through the incision already present. At present we prefer to try this prior to the retrograde flush and to reserve the latter for occasional use. Both methods will no doubt prove useful in ensuring patent distal vessels.

Postoperative Management.—The usual postlaparotomy therapy is used. Several points in particular are worthy of discussion.

Should early anticoagulation be used?

Although we earlier followed others' recommendation to heparinize immediately after embolectomy,[36,38,59] and one of us (W. A. D.) had had a small experience with regional heparinization, as described by Freeman, Wylie, and Gilfillan,[21] we now believe this to be unnecessary after adequate luminal clearance and delicate arteriotomy closure in large-vessel surgery.

Ohlwiler[40] showed in the laboratory here that heparinization could be maintained on a regional basis for only a short time before it became generalized, in terms of clotting-time elevation; so we abandoned that therapy. The complications associated with immediate heparinization[8,9,13,34] in terms of wound bleeding, hematoma, and secondary infection appear to outweigh its possible advantages after most embolectomies.

On the other hand, there are certain cases in which atherosclerotic intimal thickening, intimal damage associated with embolectomy (which may become a thromboendarterectomy) and small vessel size may strongly indicate immediate anticoagulation. Such a case occurred in which femoral thromboembolectomy in an extremely diseased vessel resulted three times in acute thrombosis upon vessel closure. After 50 mg. of aqueous heparin sodium was given, the closure was done, with the flow and distal pulse maintained well for five days, while the patient was on heparin. Cerebral hemorrhage then occurred, no doubt as a heparin complication, with death. Some such arterial cases

will nonetheless still require heparin despite the risks involved.

Should long-term anticoagulation be used?

The recurrence of peripheral embolism in other reports, as well as in one of these patients (Case 1), long after mitral commissurotomy and atrial appendectomy raises the question whether long-term slow-acting anticoagulant therapy, such as bishydroxycoumarin or ethyl biscoumacetate should be used. Warren, Linton, and Scannell [62] discussed this briefly in 1954 before the American Surgical Association and reported that 2 of their 20 patients on long-term anticoagulant therapy there was embolism within a week of cessation of therapy. In Case 2 reported here had an episode elsewhere following cessation of drug that undoubtedly was a small embolism.

After lengthy discussions of whether long-term anticoagulant therapy is indicated, we do not use it because it appears that the difficulty in time and expense and the (slight) risk of the drugs outweigh the expected decrease in incidence of later embolism.

Should lumbar sympathectomy accompany aortic embolectomy?

We did not perform sympathectomy in any of the reported cases except the first, concentrating all efforts, instead, upon restoring arterial patency not only at the bifurcation level but also to the distal vessels. Taylor [56] apparently followed the same reasoning, for, although he concluded from his review that lumbar sympathectomy should be done at the same time, he did not use it in his own successful case because he had demonstrated good blood flow. Whether sympathectomy will save life or limb if the embolectomy does not adequately clear the vessels seems doubtful. Therefore, although we do not object to it if easily done, we do not strongly advocate sympathectomy or use it routinely.

The Place of Mitral Commissurotomy.—It is doubtful that anticoagulants can be safely and practically maintained for life in many patients, and, therefore, more reliance must be placed on conversion of fibrillation and on mitral commissurotomy and atrial appendectomy than on anticoagulant therapy.

De Takats [16] reported no late recurrences of embolism after about 200 mitral operations by several surgeons and thought that the operation was "fairly protective for emboli from the left side of the heart and is preferable to long-term anticoagulant therapy." Late recurrent embolism after mitral commissurotomy and atrial appendectomy doses, of course, occur. Warren and associates [62] reported three such cases in 1954, and our Case 1 had later peripheral embolism. Grossman, Kantrowitz, Burack, and Haimovici [24] and Schein, Hoffert, and Hurwitt [49] reported late embolism after mitral commissurotomy. However, these cases of late embolism are fewer in number than if the operation were not done. Belcher and Somerville,[5] for instance, found less than a 1% incidence of postvalvulotomy embolism in 430 collected cases of mitral valvulotomy. Thus, mitral valvulotomy and atrial obliteration are indicated if the embolus originated in connection with mitral valvular stenosis.

Summary and Conclusions

A review of reported experience indicates that successful aortic embolectomy is still unusual.

To myocardial infarction and rheumatic mitral stenosis with atrial fibrillation must be added the operation of mitral commissurotomy as a common cause of aortic embolism.

The clinical syndrome of peripheral paresthesias, pain, and loss of arterial pulsations indicates immediate operation for aortic embolism, since nonoperative therapy endangers life and limb.

Operative technique and postoperative management are discussed in relation to the literature, as well as to five aortic emboli occurring in three patients herein reported.

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Fate of Human Aortic Homografts Ten, Twenty-Four, and Twenty-Seven Months After Transplantation

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The use of aortic homografts in the treatment of aneurysmal or occlusive aortic disease is well established.[5,7,9,12,14,17] Experimental studies[1,2,11,16,18,19,21-23] concerning the long-term fate of arterial homografts in animals have shown a definite pattern of response—namely, the homograft serves well as an inert, nonviable blood-carrying conduit while undergoing a gradual process of degeneration and partial replacement by an invasive and circumferential growth of fibrous connective tissue from the host.

Observations concerning the fate of human aortic homografts have been few. Gwathmey[13] has reported the occurrence of aneurysm formation due to subacute bacterial infection in a human aortic homograft five months after transplantation, and others[9] have expressed concern regarding the occurrence of late degenerative changes which have resulted in various complications. De Bakey,[6] in a study of 10 aortic homografts from 1 to 360 days after transplantation, observed that the human aortic homograft loses its structural identity and in part is replaced by connective tissues of the host, functional integrity being maintained in the meantime by persistence of

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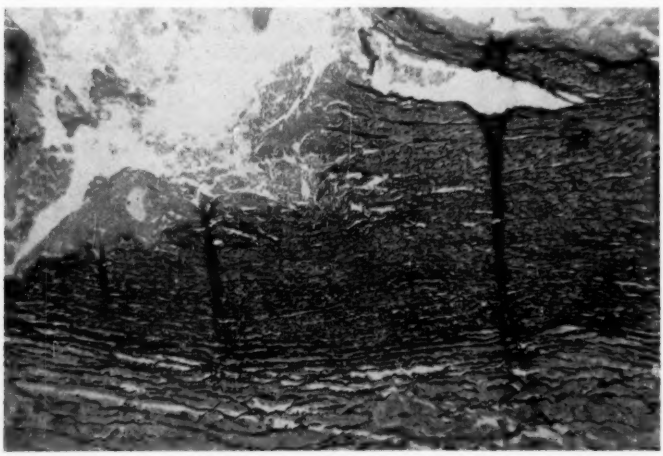

Fig. 1.—Section of 27-month-old homograft, illustrating disruption of the elastic tissue of the media by infiltrating atheromatous degeneration. With the removal of the atheromatous debris this could resemble the attenuated homograft seen in Figure 2. Verhoeff-Van Gieson stain; reduced to 61% of mag. × 100.

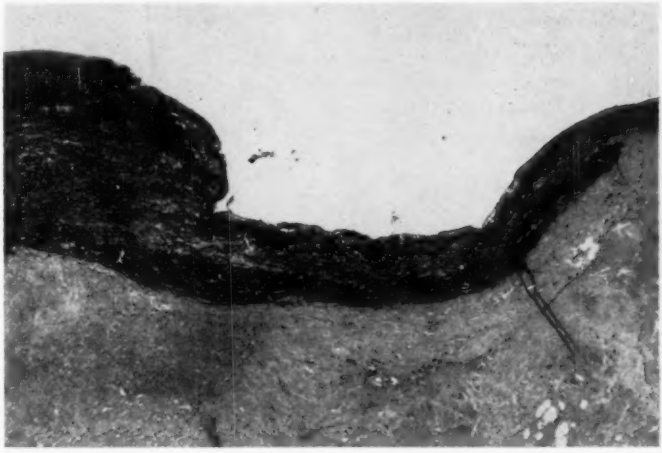

Fig. 2.—Section of aorta from 10-month-old homograft, illustrating abrupt thinning of the elastic tissue of the media, with a few lipophages seen among the elastic fibrils at the base of the first part of the attenuation. This is possibly a later stage of the process illustrated in Figure 2. Verhoeff-Van Gieson stain; reduced to 61% of mag. × 50.

the elastic fibers. In the one graft 360 days old, no retrogressive changes were seen. Later, Creech et al.[3] reported the occurrence of focal fragmentation of elastic fibers, cholesterol clefts, and scattered calcification in homografts 14, 24, and 28 months old. In the 24-month-old graft aneurysmal dilatation occurred at each anastomotic site, but in a 30-month-old, short graft no changes were seen.

In order to add further to this cumulative experience, it seems desirable to report our observations concerning the structural changes and fate of three human aortic homografts which recently became available for study 10, 24, and 27 months after transplantation.

Aortic Homografts Twenty-Four and Ten Months After Transplantation

CASE 1.—A 64-year-old white man was admitted to Hermann Hospital on Feb. 2, 1954, complaining of pain in the right upper quadrant of the abdomen, radiating into the right posterior lumbar region and around the flank into the right groin. The patient had undergone a bilateral inguinal herniorrhaphy about four weeks previously. He also had a history of an old posterior myocardial infarct; however, he was not taking any cardiac medication.

The most significant physical finding was an easily palpable, pulsatile abdominal mass arising in the midline above the umbilicus and extending to the right under the rectus muscle. The femoral, popliteal, and pedal pulses were good. Blood pressure was 130/80 mm. Hg.

Laboratory findings were not significant. An aortogram was made, confirming the diagnosis of an aortic aneurysm arising from the abdominal aorta below the renal arteries but not involving the bifurcation.

On Feb. 5, under spinal and general anesthesia, the abdomen was explored through a left paramedian incision. The aneurysm was exposed and was found to involve the aorta from 2 cm. below the renal arteries to about 2 cm. above the bifurcation. It was displacing the right ureter laterally and pressing firmly against the inferior vena cava. After it had been mobilized, it was removed between clamps and replaced with an aortic homograft. This homograft had been obtained at sterile autopsy six hours after death from a 35-year-old Negro woman who died accidentally. It had been preserved in nutrient-electrolyte medium (Gross[12]) at 4 C for 55 days. The anastomoses were made using continuous over-and-over sutures of 0000 arterial silk, interrupted twice. The period of total occlusion was 50 minutes. Pulsations were good in both extremities.

The postoperative course was uneventful, and the patient was dismissed on the 21st postoperative day. The patient was seen at monthly intervals for 12 months, and then at 3-month intervals. Pulsations remained good in both lower extremities. Palpation of the grafted aorta through a rather flaccid abdominal wall was easily accomplished, and no change in size of the graft was discernible. The patient underwent a routine check-up examination on Jan. 3, 1956, which was negative. The graft palpably seemed slightly wider than before, but not to a significant degree. On Feb. 8, 1956, the patient was in a serious automobile accident and complained of lower quadrant abdominal pain and back pain. The blood pressure was 106/90, and

there was no evidence of shock. The abdomen was tender and slightly distended, so that it was difficult to outline the aorta. During observation for 24 hours, the patient began vomiting, and examination of the abdomen revealed a definite large, tender, pulsatile mass occupying the region of the aorta. There was observed a drop in the hemoglobin from 13 to 8.5 gm.%, and a diagnosis of leaking aortic graft was made. The patient was given a transfusion, and on Feb. 10 an exploratory laparotomy was done, revealing the presence of a large, hemorrhagic, pulsatile mass retroperitoneally. Before any mobilization was begun, a trickle of bright red blood appeared on the anterior surface of the mass and then suddenly became a torrent. The blood pressure fell to 0/0. The aorta was quickly compressed against the vertebrae high in the abdomen. The aorta above the graft, but below the renal arteries, was exposed and a clamp applied. Rapid blood transfusion restored the blood pressure to about 80/50. The aorta, just proximal to the bifurcation, was exposed and clamped, and the intervening graft was excised.

A lyophilized homograft was inserted and functioned well. The total occlusion time was 80 minutes, and pulses were immediately palpable in the lower extremities. This homograft was obtained from a 23-year-old soldier three hours after death and had been sterilized with ethylene oxide and lyophilized. The new homograft bowed more anteriorly and laterally than seemed desirable because of excessive length. Owing to the exigency of the situation, a broad sling of compressed polyvinyl formalinized (Ivalon) sponge was placed around the homograft and tacked to the adjacent connective tissues to effect straightening of the graft. A more desirable solution, but requiring more time, would have been to shorten the graft and anastomose it to itself, as later events will show.

The patient made an uneventful recovery and had good pulsations on dismissal from the hospital. He returned to work about two months postoperatively, and was again followed closely and remained well. About six months postoperatively, he began to complain of low back pain. Examination at this time revealed the aorta to feel about 1 in. wide. In August, 1956, the patient was placed on chronic anticoagulant therapy for coronary artery disease. In October, 1956, he complained of pain in the upper back bilaterally. The aorta felt as if it was deviated to the left and about 1½ to 2 in. wide. Pressure on it caused pain or a burning sensation in the left upper thigh. On Nov. 9, or 10 months postoperatively, the patient had severe, agonizing back pain, and examination revealed a definite aneurysmal expansion of the aorta. On that same day, the patient was readmitted to Hermann Hospital, and a laparotomy was done. A large aneurysmal dilation of the graft was found. This was resected and replaced with a compressed, molded Ivalon tube. Function was satisfactory, and the patient recovered uneventfully and has again returned to work.

Pathological Findings in Twenty-Four-Month-Old Graft.—There was aneurysmal dilatation of the central portion of the graft, beginning about 2 cm. distal to the proximal suture line and extending to about 2 cm. from the distal suture line. There was a laceration across the anterior surface of the aneurysm. The parietal peritoneum and root of the mesentery had been dissected away by the extravasated blood on the anterior and left sides of the graft, but were densely adherent elsewhere, forming a thin fibrous-tissue sheath. At either end, the graft resembled normal aorta, and, except for the faintly visible row of black silk sutures, blended smoothly into the host vessel.

Microscopic examination is reported as follows: Sections taken through the anastomotic lines of the removed homograft revealed residual suture material, about which there was minimal foreign-body reaction. The intima over this site was considerably thickened. The media of the homograft was thin, and discontinuous at a site of atheromatous degeneration. Approaching the site of the rupture, the media diminished to consist of only a few strands of elastic tissue. The graft then consisted of a fibrocollagenous tube infiltrated with lymphocytes, through which coursed thick-walled blood vessels.

Sections of the homograft on the side away from the site of rupture revealed in the first portion well-preserved elastica in the acellular media. The adventitia was composed of dense fibrocollagenous tissue twice the thickness of the media. At a point approximately halfway along the homograft, the elastica ended abruptly in an area of atheromatous degeneration.

Pathological Findings in Ten-Month-Old Graft. Gross examination of this specimen revealed a smooth union of host aorta to each end of the graft. There was marked and densely adherent fibrous connective tissue surrounding the graft at both the proximal and the distal end. At the point where the Ivalon sling had previously been positioned, there were an abrupt dilatation and aneurysmal swelling. Examination of the inner side of the graft at this point revealed a clean-cut edge, which we interpreted as representing an area of pressure necrosis caused by continual pulsatile trauma against the immobile Ivalon sling.

Microscopic Examination of this graft is reported as follows: Section of the anastomosis between the aorta and this homograft showed some fibrous-tissue proliferation with sparse in-

filtrations of acute inflammatory cells. The intimal surfaces of both graft and host aorta were covered by fibrin and infiltrating polymorphonuclear cells.

The homograft proximal to the site of abrupt dilatation was surrounded by dense fibrocollagenous tissue and had a well-preserved elastic media with acellular fibrous connective tissue between the elastic fibrils. At the site of the dilatation, the media was infiltrated by macrophages laden with globular yellowish pigment and finely granular eosinophilic material. At this site the elastica abruptly became one-half as thick as it was previously and continued for only approximately 5 cm. before fraying out into dense fibrous connective tissue, composing the adventitia.

Section through the aorta at the point where the Ivalon sling was applied revealed the homograft to have a fairly well-preserved media with occasional focal infiltrations of macrophages; the intimal surface was covered by loose fibrous connective tissue. At the point where the Ivalon became visible in the thick sclerotic adventitia, there was an abrupt break in the elastica of the homograft, and the Ivalon was covered directly by fibrin and loose fibrous connective tissue. The Ivalon on hematoxylin and eosin preparations was translucent, and within the interstices were numerous polymorphonuclear cells in a fibrin meshwork. The Ivalon continued only a short distance and it, too, disappeared, and the wall of the dilated vessel consisted only of fibrocollagenous tissue of the adventitia covered with fibrin and leukocytes and with an occasional remnant of elastica.

Aortic Homograft Twenty-Seven Months After Transplantation

CASE 2.—A 60-year-old white man was admitted to Southern Pacific Hospital on March 1, 1954, complaining of vague abdominal and moderately severe back pain of about three months' duration. He gave a past history of angina pectoris and asthma. Palpation of the abdomen revealed the presence of a moderately large, slightly tender, pulsatile abdominal mass in the midepigastrium. The femoral, popliteal, dorsalis pedis, and posterior tibial pulses were normal. Blood pressure was 160/90 mm. Hg. Examination of the chest showed many musical rales bilaterally, and the expiratory effort was prolonged and labored. There were evidence of pulmonary emphysema and a chronic productive cough. Intravenous pyelograms were normal, but revealed a soft-tissue shadow faintly circumscribed with calcium in the region of the abdominal aorta.

The patient was placed on a medical regimen designed to control the asthma and chronic bronchitis. On March 10, an exploratory laparotomy was done, and a fusiform aneurysm of the abdominal aorta was found, which involved the bifurcation and originated 2 cm. below the renal arteries. After it had been mobilized, the aneurysm was removed between clamps and replaced with a lyophilized aortic homograft, including the bifurcation. The occlusion time was 60 minutes, and, upon release of the clamps, pulsations were good in both lower extremities. This homograft had been obtained five hours after death at unsterile autopsy on a 22-year-old man who died accidentally. It was sterilized with ethylene oxide and lyophilized.

The patient made an uneventful recovery and was dismissed from the hospital on the 12th postoperative day. He returned to work as an accountant, and was seen periodically in the outpatient clinic. In May, 1956, he was readmitted to the hospital and died of a severe, uncontrollable asthmatic attack and congestive heart failure.

An autopsy was obtained, and the report follows. Microscopic examination of the homograft at the anastomotic lines revealed the juxtaposition of an acellular, elastic media of the homograft with the atheromatous aorta. At the point of approximation some suture material was seen, about which there was a scanty infiltration of lymphocytes and the formation of some giant cells of the foreign-body type. There was a wedge-shaped defect in the intima, which was filled in with fibrocollagenous tissue containing numerous small, cleft-like spaces. These were filled with a lightly basophilic amorphous material infiltrated with lymphocytes. This fibrocollagenous tissue extended over the surface of the homograft for a 2 cm. length. This thickened, fibrocollagenous intima was infiltrated with lipophages, forming small foci of atheromatous degeneration in the intima of the homograft. This intima was approximately the thickness of the media throughout this section. The adventitia consisted of moderately dense fibrocollagenous tissue with focal lymphocytic infiltrations. An occasional capillary was seen in the outer one-fifth of the media.

The fibrocollagenous intimal tissue became thinner and less cellular as it coursed down the homograft.

Sections of the homograft taken near the midportion revealed an essentially acellular, elastic media, which contained foci of dense calcium deposition, and the media was covered on the intimal surface by fibrocollagenous proliferation, containing numerous small clefts filled with calcium. The adventitia was approximately as thick as the media. Some lipophage infiltration was also noted in the homograft sections.

Summary and Conclusion

The long-term fate of human aortic homografts is of interest to all who are employing this method of treatment for certain aortic diseases.

This report illustrates the occurrence of definite aneurysmal dilatation 24 months after transplantation of one aortic homograft preserved in Gross' medium. Microscopically, there were degeneration, fragmentation, and loss of elastic fibers at the site of the aneurysm, and arteriosclerotic changes were present throughout the graft.

A second lyophilized homograft developed an aneurysm after 10 months, owing to pressure necrosis caused by an Ivalon sling. Microscopic study of this specimen revealed little structural degeneration and good union to the host aorta, except at the site of continued pulsatile trauma.

A third lyophilized homograft functioned perfectly for 27 months, until the death of the patient, from unrelated causes. Postmortem examination revealed moderately advanced atheromatous changes in the homograft similar to those in the host aorta. Interestingly enough, serum cholesterol levels in this patient were normal.

Various studies [1,2,15-19,21-23] of animal aortic homografts have demonstrated the frequent occurrence of calcification, intimal lipid deposition, atheromatous plaques, and fibrosis. Swan et al.[22] recorded the presence of intimal macrophages, as well as calcification, in the homografts of dogs after five months. Sauvage and Wesolowski [19] concluded from their studies in the pig that arteriosclerosis was no more prone to occur in autografts than in the host vessels, but that homografts show a greater tendency toward such change. Fisher and Fisher [10] noted a marked susceptibility to arteriosclerosis in fresh and lyophilized aortic homografts in rabbits with experimentally induced cholesterol arteriosclerosis, and Creech [4] demonstrated the same occurrence in dogs.

It is a known fact that the development of such experimental arteriosclerosis is enhanced in damaged or altered vessels. Certainly, homografts can be considered to be in this category. It is logical to assume that a homograft will undergo the same degenerative processes that affect the host vessels when they are subjected to the same factors and influences. In a sense, homografts are a locus minoris resistentiae. In fact, one might expect such degenerative changes to develop more rapidly in homografts than in the patient's own vessels. Whatever the fundamental causes of the atheromatous form of arteriosclerosis, they apparently require between 30 and 50 years to produce their effect on the autogenous arterial system. Creech et al.[3] reported retrogressive changes characteristic of arteriosclerosis in three aortic homografts, 14, 24, and 28 months old. In two of the grafts described in our report, one 24 and one 27 months old, definite arteriosclerotic changes were seen. In two of these five homografts, definite aneurysmal dilatation had occurred. It is interesting to note that in our Case 2 a lyophilized aortic homograft developed in a period of 27 months a degree of arteriosclerotic change equal to that seen in the patient's own vessels developed over a period of 60 years.

It would seem from these observations that aortic homografts undergo a process of degeneration and develop arteriosclerotic changes to a varying degree as time goes by. Despite these observed structural changes, most animal homografts have maintained their functional integrity for periods of several years. In fact, the first human aortic homografts implanted by Gross [12] in the treatment of coarctation of the aorta are said to be functioning well nine years after implantation. This study preceded the reports of Oudot [17] and Dubost,[8] which extended the use of aortic homografts to the treatment of acquired occlusive and aneurysmal aortic disease. De Bakey and Cooley [5] subsequently ap-

plied this method of therapy to a large number of patients.

Undoubtedly, many aortic homografts will ultimately develop progressive arteriosclerotic degenerative changes in varying degree, but, owing to the adaptative response of the host, will maintain their functional objective for the lifetime of the patient. A yet undetermined percentage will ultimately fail because of aneurysm formation or occlusion. As the result of an excellent study, Szilagyi [20] has estimated that the majority of aortic homografts will remain free from changes serious enough to threaten function for probably as long as five years; however, after this time, a significant incidence of aneurysm formation may be expected. Arteriosclerotic aortic disease is found almost always at autopsy in patients over 40, but only a few actually develop clinically significant aneurysms or occlusion. Such will probably prove true of homografts also. Presently available knowledge indicates that these changes, resulting in functional failure, will take a relatively long time for their development, and perhaps will occur in the minority, and therefore should not interdict the continued use of homografts as availability permits or until a better substitute is found. In fact, the dual problem, today, concerning arterial replacement is primarily with the difficulty of procurement, preparation, and preservation of homografts and the question of their durability, as raised by observed changes such as those reported in this paper. It is indeed these problems which have led to a search for a readily available, functionally equal, technically feasible, and more durable synthetic substitute.

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Cardiovascular and Hemodynamic Functions in Dogs Subject to Prolonged Aortic Occlusion

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Obstruction of the thoracic aorta for 30 minutes can be accomplished without apparent damage to the animal.[1] When the period of occlusion is greater than 30 minutes, spinal cord damage, manifested by hindlimb paralysis, ensues in a large percentage of cases. There is a progressive increase in the percentage mortality as the length of obstruction is prolonged. Although survival studies following prolonged aortic obstruction and autopsy reports have been presented, relatively few investigations have been conducted on the alterations in the cardiovascular functions. Studies of the hemodynamic and metabolic changes occurring consequent to prolonged occlusion of the thoracic aorta have been made and are being reported herein.

Methods

Eleven mongrel dogs, ranging in weight from 11.2 to 19.5 kg. (mean body weight, 14.9 kg.) were anesthetized with pentobarbital sodium (30 mg/kg. body weight) and heparinized (5 mg/kg. body weight). A single-lumen, bird's-eye-tip cardiac catheter was inserted into a branch of a jugular vein and positioned in the main pulmonary artery under fluoroscopic guidance. A triple-lumen cardiac catheter with an inflatable balloon affixed 1 in. from the tip was inserted into the femoral artery and advanced into the descending aorta so that the balloon rested at the fourth rib interspace. Aortic obstruction could then be accomplished by inflating the balloon with 4 ml. of iodopyracet (Diodrast)-saline solution. Complete obstruction was confirmed by a fall in the arterial pressure below the balloon to 16 mm. Hg.[2] Blood pressures were recorded throughout the experiment from the pulmonary artery and the aorta both above and below the obstructing balloon with the aid of Statham pressure transducers and appropriate amplifying and recording equipment. The right atrium served as the point of zero-pressure reference. Oxygen consumption was measured with a Benedict-Roth metabolism apparatus. Blood samples were drawn from the aorta above the obstructing balloon and the pulmonary artery for the determination of oxygen and carbon dioxide content by the method of Van Slyke and Neill.[3] Cardiac output was calculated by the direct Fick principle.

After the withdrawal of blood samples for control values, the aorta was obstructed. Blood samples were drawn at hourly intervals during the obstruction period. A five-hour obstruction period was the maximum length attempted, although in several instances the obstruction was released earlier. If the animal was alive at the end of five hours, the obstruction was released and the animal was either killed for autopsy studies or allowed to survive. Autopsies and histological studies were performed on all animals which died or were killed.

The data were subjected to statistical analysis, utilizing the paired *t*-test. The null hypothesis was rejected at the 5% level of significance.

Results

The aorta was obstructed for various periods of time ranging from 136 to 306 minutes, the average time of obstruction being 226 minutes. Four animals died during the obstruction period, but in the remaining seven it was possible to continue the experiment through the release of the obstruction. Of these seven animals, two were killed at the time of release, two died within 10 minutes after release of the occlusion, two died within 24 hours, and one survived but was killed 4 days after the

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Alterations in Metabolic Functions Consequent to Prolonged Occlusion of Thoracic Aorta at Fourth Rib Interspace

	Control	Period of Occlusion, Hr. 1	2	3	4
Arterial O_2 content, vol. %	17.2	19.2	18.4	18.3	17.8
Arterial-MV * O_2 difference, vol. %	4.48	5.76	6.47	8.26	8.39
Oxygen consumption, ml/min.	84	49	55	40	46
Cardiac output, L/min.	2.01	1.10	0.98	0.86	0.43
Arterial CO_2 content, vol. %	44.81	35.12	32.52	36.09	30.00
MV CO_2 content, vol. %	47.28	39.78	37.75	40.22	37.33
Mean arterial pressure above balloon, mm. Hg	114	154	136	127	119
Mean arterial pressure below balloon, mm. Hg	110	15	15	15	15
Pulmonary artery systolic pressure, mm. Hg	16.2	24.3	18.7	15.4	21.3
Pulmonary artery diastolic pressure, mm. Hg	7.3	15.0	13.3	10.3	16.5
Heart rate, beats per min.	163	139	143	131	126
Peripheral vascular resistance, units	4333	1119	1109	1180	2212

* Arterial-mixed venous O_2 difference.

experiment. Ventricular fibrillation was observed in both of the animals which died soon after release of the occlusion. Of the three animals surviving the experiment for a short period of time, all showed signs of neurological damage. The animal which was killed at four days was unable to stand and was in apparent pain. In those animals which died during the obstruction, respiratory arrest occurred, followed shortly by cardiac arrest.

The hemodynamic and metabolic data are presented in the accompanying Table. As very few animals survived beyond four hours, the data were statistically analyzed for only the first four hours of occlusion.

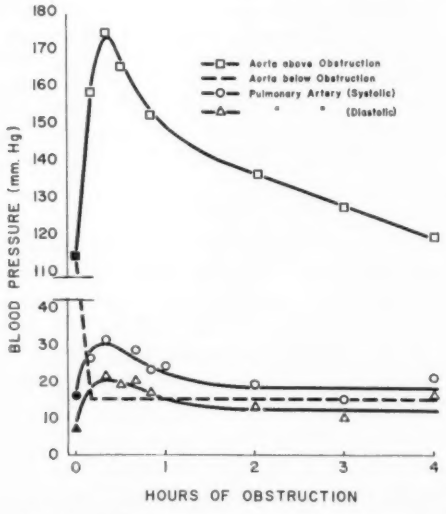

Fig. 1.—Blood pressure changes consequent to occlusion of the thoracic aorta at the fourth rib interspace for a four-hour period.

The blood pressure relationships are illustrated in Figure 1. The control mean arterial blood pressure was 114 mm. Hg. Following inflation of the balloon the pressure in the aorta below the balloon was 15 mm. Hg and remained at this level until release of the obstruction. The pressure in the aorta above the obstruction rose sharply, reaching a peak of 174 mm. Hg at 20 minutes of obstruction. The arterial pressure above the balloon gradually decreased toward control values during the obstruction but remained significantly elevated above

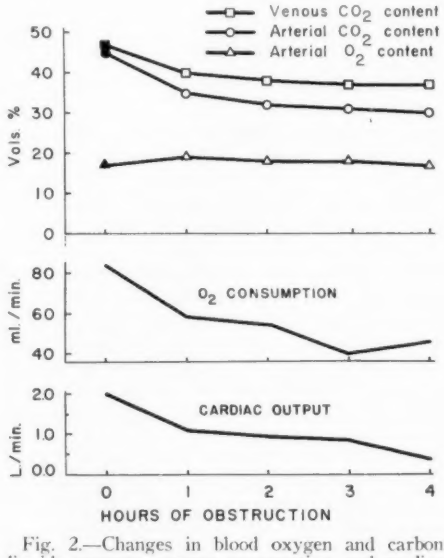

Fig. 2.—Changes in blood oxygen and carbon dioxide contents, oxygen consumption, and cardiac output which occurred after a four-hour obstruction of the thoracic aorta at the fourth rib interspace. The values at zero hour are the control levels.

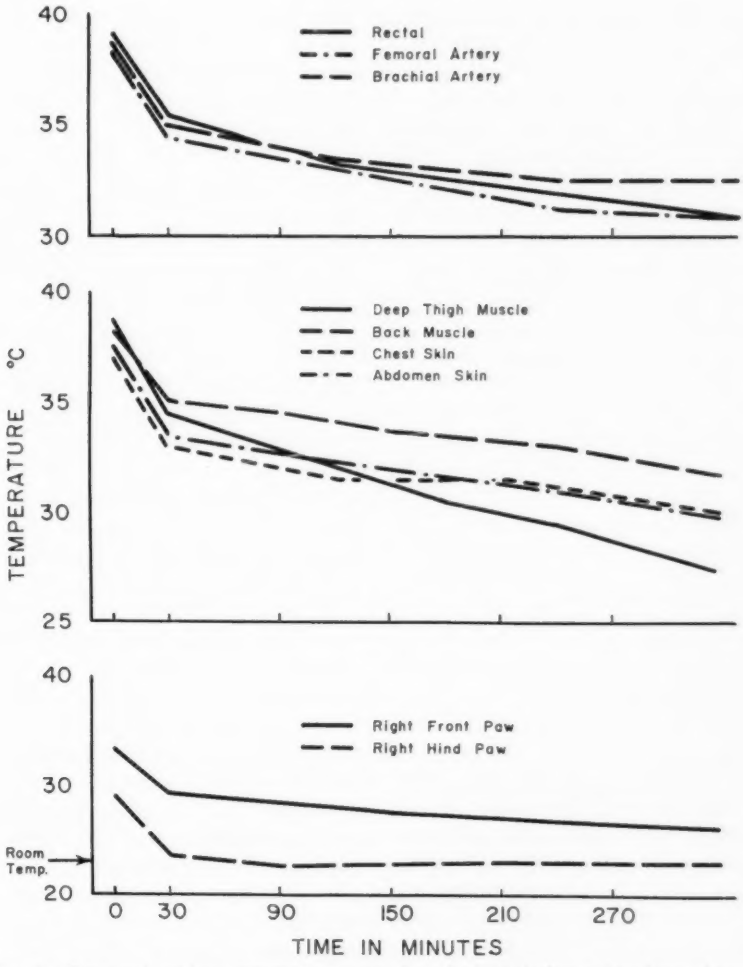

Fig. 3.—Deep and surface temperatures of a dog obtained during a four-hour obstruction of the thoracic aorta at the fourth rib interspace.

control levels for the first three hours of obstruction. After release of the obstruction this pressure dropped precipitously and remained below control levels. In those animals which died during the obstructive period, the blood pressure remained at a high level until shortly before death but fell rapidly with the occurrence of cardiac arrest. Respiratory arrest preceded cardiac arrest in most animals. The pulmonary arterial systolic pressure was 16.2 mm. Hg during the control period and was increased to 25.9 mm. Hg after 10 minutes of obstruction. This pressure remained significantly elevated throughout the first hour of occlusion but had returned to within the control range during the remainder of the experiment. The pulmonary arterial diastolic pressure followed a similar pattern, the control value being 7.3 mm. Hg and the maximum level 21.0 mm. Hg at 20 minutes of occlusion. The heart rate fell from a control value of 163 beats per minute to 134 beats per minute and stayed at this lower level during the entire experiment.

The metabolic relationships are presented in graphic form in Figure 2. The arterial oxygen content (drawn from the aorta above the obstructing balloon) was not altered as a result of the occlusion. Both arterial and pulmonary arterial carbon dioxide contents were decreased significantly at one hour of occlusion and continued to decrease throughout the obstruction period. The mixed venous oxygen content appeared to show a slight decrease, but no change could be demonstrated by statistical analysis. Total oxygen consumption and cardiac output fell markedly and progressively throughout the obstruction period. Four animals showed periods of apnea, which were accompanied by continuous oxygen uptake. These periods of apnea always occurred within a 30-minute interval immediately prior to death. All animals which exhibited the bouts of apnea succumbed during the experiment.

Temperatures were recorded from several sites during an obstruction of 288 minutes' duration in one animal. The alterations in temperature are recorded in Figure 3. All of the temperatures recorded from various areas of the body fell progressively during the occlusion, the greatest decrease occurring during the first 20 minutes of the obstruction. At the end of the obstruction, those temperatures recorded from the lower half of the body (distal to the obstructing balloon) were lower than those areas to which the arterial circulation was still intact.

Comment

An obstruction of the thoracic aorta above the origin of the celiac artery can be tolerated for approximately 30 minutes without apparent harm to the animal, but obstructions of longer periods are often detrimental.[1] Both Smith[4] and Parkins[1] and their associates have reported 100% mortality after one and one-half hours of occlusion. No attempt was made in the present series to obstruct the aorta for more than five hours. Three animals were alive at the end of this period. Only one animal was alive 24 hours after obstruction: This animal suffered considerable neurological damage and was killed after 96 hours.

Eiseman and Summers[5] have stressed the wide variation in the vascular supply of the spinal cord, which undoubtedly accounts for the variation in tolerance of animals to prolonged occlusion. Edwards and associates[9] state that the mortality rate for a given period of aortic occlusion is directly proportional to the amount of vascular bed rendered ischemic. Previous investigations[6] in this laboratory have demonstrated collateral circulation from the upper aorta to the posterior area by way of the anterior spinalis and intercostal arteries. Splanchnic blood flow during a short period of aortic obstruction was determined to be approximately 30% of the control flow. If this amount of flow is also present during an obstruction of several hours, it is apparently insufficient to prevent the development of tissue damage and leads, upon release of the obstruction, to irreversible shock. Further indication of the altered available blood supply and the development of a shock state comes from the temperature data presented in Figure 3.

The reduction in cardiac output and oxygen consumption was highly significant. However, if one evaluates the cardiac output and oxygen consumption in terms of the vascular bed being perfused (which represents approximately one-half of the total bed), the blood and oxygen supply should have been adequate. Furthermore, since the pulmonary arterial oxygen content was not appreciably changed and, consequently, the extraction of oxygen was not increased, it would appear that the oxygen needs of the perfused portion of the organism were met while the obstruction was in place. However, there is a shift in the oxygen dissociation curve, resulting in a decreased dissociation of oxyhemoglobin and a reduction in the availability of oxygen to the tissues. Smith[7] reported a fall in cardiac output from 1.52 to 1.12 liters a minute after a 95% obstruction of the aorta,

but he does not indicate the time of his measurements. Blalock [8] measured the cardiac output in dogs one hour after occluding the thoracic aorta and reported a fall from a control of 1.21 liters a minute to 0.4 liter a minute during the obstruction. These values, and those in current series, may be related to the kind of preparation employed by these different investigators.

The initial changes in arterial blood pressure are similar to those previously reported in short-term experiments. The increased pulmonary arterial blood pressures are probably a reflection of the increased systemic pressure. As the systemic pressure fell, the pulmonary arterial pressures returned toward control levels.

The fall in arterial and venous carbon dioxide contents was marked. Blalock [8] reported this same phenomenon in the one animal he so studied. The significant decrease in blood carbon dioxide cannot be readily explained except as an index of the total decrease in metabolism.

Summary

The thoracic aorta was obstructed at the fourth rib interspace for varying periods of time ranging from 130 to 300 minutes. Three animals were alive after five hours of obstruction, and they all exhibited signs of neurological damage. The cardiac output and oxygen consumption decreased progressively throughout the obstruction period. There was little or no change in arterial and mixed venous blood oxygen contents, but there was a progressive and marked fall in the arterial and mixed venous carbon dioxide contents.

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Sigmoidovesical Fistula Secondary to Diverticulitis

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Diverticulitis is the commonest cause of a sigmoidovesical fistula. Another inflammatory process, neoplasia, trauma, or a congenital abnormality may be responsible. A highly resistant lower urinary tract infection should suggest the possibility of an incipient or established vesico intestinal fistula. Pneumaturia and fecaluria are positive evidence of such a communication. Surgical excision of the diseased segment of colon and closure of the vesical opening is the procedure of choice. In many cases this may be carried out as a primary procedure.

General Background

History.—Cripps,[3] in 1888, found that inflammatory lesions more frequently caused sigmoidovesical fistula than did malignant lesions. Heine,[5] in 1904, and Moynihan,[11] in 1907, realized the importance of diverticulitis as an etiologic factor in these fistulae. In 1917, Telling and Gruner[15] made an extensive study of diverticulosis and diverticulitis and observed that in 19.8% of the cases reviewed some type of fistula was present. From his review of the literature, Arnheim,[2] in 1940, concluded that approximately 8% of cases with diverticulitis have a sigmoidovesical fistula. Mayo and Blunt,[10] in 1950, found an incidence of vesicosigmoidal fistula of 22.8% in patients requiring an operative procedure for a complication of diverticulitis. Evaluation of a similar group by Ransom,[13] in 1954, disclosed an incidence of vesicosigmoidal fistula of 10%. Reid and Workman,[14] in 1955, analyzed 266 cases of diverticulitis requiring hospitalization. The incidence of vesicocolonic fistula in this group was 1.5%.

Clinical Features.—Sigmoidovesical fistula secondary to diverticulitis is commoner in males than in females. Diverticula of the colon occur one and a half times as frequently in males. In females the interposed uterus and adnexa provide a barrier to a sigmoidovesical fistula. The usual patient is in the sixth decade of life, and the condition is rare under the age of 40.

Numerous authors have noted that with many of these patients the prominent symptoms were those of disease of the urinary tract, while the intestinal symptoms were minimal or, indeed, frequently absent. Mayfield and Waugh[8] found that the average duration of abdominal symptoms, when present, prior to the establishment of the fistula was three years and three months. The intestinal symptoms—primarily pain and constipation or diarrhea—not infrequently regress after development of the fistula.

The outstanding and cardinal symptom of a vesicointestinal fistula is pneumaturia or the passage of free gas from the urethra. This gas may be accompanied by fecal material. Frequently, however, the fistulous tract may be small and tortuous and does not permit the passage of solids from the intestinal tract to the urinary bladder. The urine may reveal fragments of food or more readily identifiable ingested substances, such as liquid petrolatum U. S. P. (mineral oil) or plantago seed N. F. (psyllium seeds). The passage of urine from the bladder into the

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bowel, in a vesicointestinal fistula, is uncommon, and we have never seen this occur. Intrarectal and sigmoidal pressure far exceeds the intravesical pressure. The most frequent cause of vesicointestinal fistulae has been the rupture of diverticular abscesses, which have become adherent to the bladder. Second in frequency, carcinoma of the bladder or the rectum may erode into one or the other. We have seen one instance of an appendiceal abscess rupturing into the bladder, causing pneumaturia, and also one fistula involving the renal pelvis and the transverse portion of the colon.

Other causes of pneumaturia include the introduction of air during instrumentation and fermentation within the bladder. We have rarely observed gas fermentation in the bladder. For such a condition the urine must usually contain an excess of sugar, as in diabetes, and usually a yeast organism of the Saccharomycetes type is present. Pneumaturia is most uncommon with the usual bladder infections.

Urinary frequency, urgency, burning, pyuria, and albuminuria may herald an incipient stage, as the inflammatory process lies adjacent to the bladder. Marked frequency of urination in a patient with diverticulitis suggests that a urinary fistula may be developing. When the communication is relatively complete, sudden severe tenesmus and stranguria may be present. The usual history is one of passing gas, and possibly feces, via the urinary tract, with concomitant urgency, frequency, and dysuria due to the associated cystitis. Infection of the upper part of the urinary tract is an infrequent complication.

Cystoscopy may be of value in establishing the diagnosis. During the incipient stage one may observe a localized area of cystitis. This generally occurs on the left side near the base of the bladder. After fistula formation there are edema, marked cystitis, and often fecal matter in the urine. The demonstration of the fistulous tract by cystoscopy is not difficult. Usually a large area of edema and inflammation surrounds the vesical orifice of the fistula. Occasionally the cystogram seen during intravenous urography will display an abnormal collection of gas in the bladder.

Proctosigmoidoscopy is seldom of diagnostic value. On occasion the fistula can be demonstrated by a cystogram or a barium enema. If the diagnosis remains in doubt, one may instill methylene blue N. F. or sodium indigotindisulfonate U. S. P. (indigo carmine) in the bladder and recover it in the stool. Charcoal taken orally may be recovered in the urine.

Treatment.—In 1940, Mayo [9] discussed the surgical treatment of sigmoidovesical fistula in 54 cases. Diverticulitis was the cause in 59%. He concluded that a proximal colostomy should precede any surgical attack upon the fistula. This opinion was held by Jones [6] in 1936; Dixon [4] in 1939; Pemberton [12] in 1945; Mayfield and Waugh [8] in 1949; Welch, Allen, and Donaldson [16] in 1953, and Abeshouse and associates [1] in 1957. However, in recent years an increasing number of primary resections have been performed for diverticulitis. Judd and Smith,[7] in a recent report, stated that 24% of 113 patients undergoing a one-stage resection for diverticulitis had some type of a fistula.

Report of Cases

CASE 1.—A 52-year-old woman was admitted to the hospital on July 25, 1954, with a two-year history of urinary frequency, nocturia, periodic hematuria, a constant brownish discoloration of the urine, and intermittent passage of air with the urine. Episodic chills and fever had been present. She also stated that on several occasions liquid petrolatum, taken orally, had appeared in her urine. Intermittent lower abdominal pain and constipation had been present for five years and required frequent laxatives and enemas. Three years prior to admission she had a minor episode of bright red rectal bleeding. A hysterectomy had been performed in 1934. Bladder polyps were fulgurated in 1951 and 1952.

Physical examination revealed a well-nourished, middle-aged woman, not acutely ill. The temperature was 99 F, and the blood pressure was 172/94. Abdominal examination was negative. The hemoglobin was 9.5 gm.%, and the leukocyte count was 4500 per cubic millimeter. The blood urea

nitrogen was 12.5 mg.%. Microscopic examination of the urine showed many pus cells, and the urine culture was positive for nonhemolytic (gamma) streptococci. The excretory urogram was normal. With barium enema the contrast medium would not pass beyond the midsigmoid area, although the cause of the obstruction could not be determined.

Cystoscopy was performed on July 26, 1954. A granulomatous mass, pushing from without, involved the floor of the bladder adjacent to the left ureteral orifice. On its superior aspect an irregular area was seen with a piece of debris protruding therefrom. This was felt to represent a vesico colonic fistula. The area bled readily on manipulation. Proctoscopy to 24 cm., on July 27, failed to reveal any pathology.

Laparotomy was performed on July 30. Ureteral catheterizations were done preceding the operation. There was considerable induration in the midsigmoid, and this area was adherent to the posterior trigonal area of the bladder. A cuff of bladder was excised at the site of the fistula, and the bladder was closed. The indurated pericolic area with approximately 6 cm. of normal bowel on either side was excised and a primary end-to-end anastomosis carried out. A suprapubic catheter and Penrose drain were brought out through the wound. The specimen showed chronic diverticulitis and peridiverticulitis. The fistula tract was not identified. Hemorrhage from about the drain site, presumably from the retroperitoneal area, was a source of concern in the immediate postoperative period. This bleeding ceased spontaneously. Her subsequent course has been entirely satisfactory.

Case 2.—A 69-year-old man was admitted to the hospital on Aug. 14, 1955, with a one-day history of passing brown particulate matter in the urine. There were associated urinary frequency, burning, and a strong fecal odor to the urine. During the preceding two weeks he had noted intermittent cramping pain in the left lower abdominal quadrant and constipation. In 1938 a diagnosis of sigmoidal diverticulitis had been made after evaluation of lower abdominal pain. He had had periodic attacks of lower abdominal pain since that time. In 1951 a transurethral resection of a benign prostatic enlargement had been performed.

Physical examination was negative except for a large, tender mass in the left lower abdomen. There was no associated rigidity. The temperature was 100.8 F. The hemoglobin was 12.0 gm.%, the leukocyte count 12,600 per cubic millimeter, and the nonprotein nitrogen 31 mg.%. The urine was loaded with white blood cells.

Laparotomy was performed on the day of admission. Exploration disclosed a large, firm, nonfluctuant mass in the left pelvis. It was not possible to determine whether this was on a malignant or an inflammatory basis. Further manipulation of the pathologic area was not deemed advisable, and a right transverse colostomy was performed. The postoperative course was uncomplicated. Proctoscopy to 18 cm. on Sept. 3 revealed fixation of the sigmoid area with many diverticula. Several polyps were present, but there was no evidence of malignancy.

The patient was readmitted on Jan. 29, 1956. The urinary symptoms had disappeared, but a definite mass was palpable in the left lower abdominal quadrant. The urine was loaded with leukocytes and on culture showed Pseudomonas aeruginosa. At exploration, on Feb. 3, the sigmoid was found to be adherent to the left lateral aspect of the bladder and enveloped in an indurated mass of omentum. The involved segment of bladder was excised and the walls aproximated. The colon showed multiple diverticula, and 35 cm. of descending colon and sigmoid, including the mass, was excised prior to end-to-end anastomosis. Pathologically, there was an area of peridiverticulitis with a demonstrable fistula in the sigmoid area. Wound dehiscence on the fourth postoperative day necessitated a secondary closure. Thereafter the course was uncomplicated.

The transverse colostomy was closed without incident on April 12, 1956. Proctoscopy on April 10, 1956, disclosed an adequate anastomosis. The nonprotein nitrogen was 25 mg.%, and urinalysis revealed but occasional leukocytes. He has had no further intestinal or urinary symptoms.

Case 3.—A 53-year-old man was admitted to the hospital on Sept. 12, 1956. On Aug. 25, 1956, he had noted the onset of chills with increase in temperature to 102 F. Shortly thereafter, there were associated urinary frequency, burning, and cloudy urine. Sulfisoxazole U. S. P. (Gantrisin) failed to provide relief. Lower abdominal cramping, pain, and obstipation appeared 10 days later. Concomitantly he noted hematuria, brownish discoloration of the urine, and passage of gas from the urethra. The pneumaturia occurred on several occasions thereafter. The urinary symptoms, chills, and fever persisted in spite of antispasmodic urinary antiseptics. In 1943, an abscess adjacent to the sigmoid had been drained. A barium enema during the postoperative period had disclosed multiple diverticula of the colon. He had been taking laxatives regularly since that time. Approximately once a year he had an episode of lower abdominal cramping pain and obstipation.

Physical examination disclosed a well-nourished middle-aged man. The blood pressure was 122/80, and the temperature was 99.4 F. Examination of the abdomen was negative. The hemoglobin was 13.8 gm.% and the the leukocyte count was 8000 per cubic millimeter. Urinalysis showed 15-20

white blood cells per high-power field and numerous red cells. The urine culture revealed a moderate growth of nonhemolytic streptococci and coliform organisms. There was also a light growth of Alcaligenes fæcalis. The excretory urogram was negative. A cystogram failed to disclose an intrinsic lesion. The barium enema demonstrated a midsigmoidal obstruction of undetermined etiology. Cystoscopic examination revealed an inflammatory process at the dome of the bladder. Proctoscopy to 24 cm. was normal except for decreased mobility of the sigmoid colon.

On Sept. 19, 1956, a laparotomy was performed. The midsigmoid was adherent to the bladder by a large inflammatory mass. The bladder was dissected free, and adjacent tissue was sutured over the inflammatory area in the dome of the bladder. An end-to-end anastomosis of the sigmoid was performed after removal of a 20 cm. section of bowel. The specimen showed multiple diverticula with acute peridiverticulitis and fistula formation in the midportion. An indwelling catheter was left in one week. The postoperative course was uncomplicated, and he has remained symptom-free.

CASE 4.—A 65-year-old man was admitted to the hospital on March 17, 1957. One month prior to admission he had noted the onset of urinary frequency and burning. The symptoms progressed to almost constant suprapubic discomfort. Since the symptom onset he had had several episodes of chills and fever, and passage of periodic gas and solid particles in the urine. He denied having had any associated or previous gastorintestinal difficulty except for mild constipation, which had been present for approximately six months. Resection of the upper lobe of the right lung has been performed in August, 1956, because of a suspected malignancy. The process proved to be inflammatory. He was taking digitalis daily because of an auricular fibrillation, diagnosed 15 months prior to admission. This was felt to be due to arteriosclerotic heart disease.

He did not appear acutely ill. The blood pressure was 130/80, with an irregular pulse of 80 a minute. Abdominal examination was negative. The hemoglobin was 13.0 gm.%, with a leukocyte count of 14,250 per cubic millimeter. The blood urea nitrogen was 14.2 mg.%. The urine culture showed a heavy growth of coliform organisms and viridens (alpha) streptococci. The excretory urogram disclosed an irregular filling defect on the left side of the bladder (Fig. 1). The upper urinary tract was negative. Barium enema revealed numerous diverticula with an irregular narrowing in the midsigmoid area. Cystoscopic examination showed marked bullous edema and inflammation on the left side of the bladder.

Fig. 1.—A cystogram, taken during excretory urography, showing a large irregular filling defect on the left. This area, adjacent to a sigmoidovesical fistula, was the site of bullous edema and inflammation.

Proctoscopy to 18 cm. disclosed numerous diverticula but no other pathologic process.

Laparotomy was carried out on March 27, 1957. The midsigmoid was adherent to the dome of the bladder by an inflammatory mass. The sigmoid was dissected free without difficulty. A definite fistulous tract could be visualized. It was not necessary to resect any of the bladder wall. Fifteen centimeters of sigmoid was resected and an end-to-end anastomosis performed. The specimen showed multiple diverticula with subacute inflammation and a fistulous tract in the midportion. The postoperative course was uncomplicated. An indwelling catheter was left in place for one week. The urinary frequency gradually subsided, and he has remained symptom-free.

CASE 5.—A 63-year-old man was admitted to the hospital on Aug. 13, 1957. For two years he had had persistent urinary frequency and burning. Periodic urine cultures disclosed a coliform infection, which failed to respond to multiple urinary antiseptics. Six months after symptom onset a transurethral resection was performed, without benefit. Intermittently since the transurethral resection he had been aware of passage of air with the urine. Chills and fever had been present at the onset of symptoms, but had not recurred. He denied any gastrointestinal symptoms. The past history was negative except for periodic attacks of gout, which responded promptly to colchicine.

Physical examination revealed a hypertension of 180/100. Abdominal evaluation was negative. The hemoglobin was 13.9 gm.%; leukocyte count 7850 per cubic millimeter, and urea nitrogen 14.8 mg.%. Urinalysis disclosed numerous white blood cells and a moderate amount of erythrocytes. Urine culture showed nonhemolytic Staphylococcus

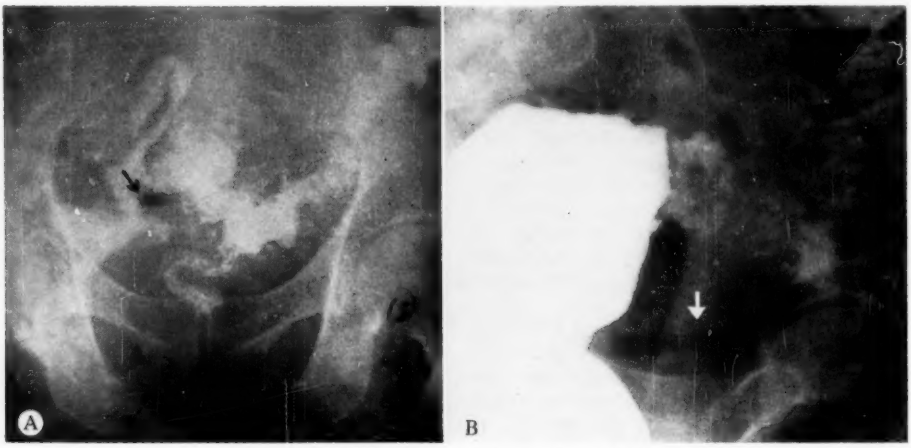

Fig. 2.—Roentgenographic evidence, during barium enema, of the air within the urinary bladder: (*A*) anteroposterior view; (*B*) oblique view.

aureus var. albus. The excretory urogram was negative. Barium enema revealed numerous diverticula of all portions of the colon. By special views air could be visualized in the urinary bladder (Fig. 2). At cystoscopy an inflamed, edematous granular area was seen in the posterior superior aspect of the bladder. Pus was exuding from the center of the area. Proctoscopy to 16 cm. showed some fixation of the rectosigmoid area, limiting further introduction of the scope. However, no definite pathologic process could be visualized.

Laparotomy was performed on Aug. 19, 1957. There were multiple fibrous adhesions between the sigmoid colon and the bladder. These were divided without difficulty. A definite fistulous tract was not visualized. Seventeen centimeters of colon was resected and a primary end-to-end resection done. The specimen showed multiple diverticula with chronic peridiverticulitis and a fistula in the midportion. An indwelling catheter was left in for six days after operation. A febrile reaction in the postoperative period disappeared after evacuation of a wound hematoma. The subsequent course was uneventful. He was discharged on Sept. 7, without symptoms and with a negative urinalysis.

Comment

We have encountered five cases of sigmoidovesical fistula secondary to diverticulitis during the past three years. Four of the patients were men; the woman had undergone a previous hysterectomy. The age range was 52 to 69, with an average of 60.

The duration of urinary symptoms varied from one day to two years, and all patients had noted chills and fever at some time during that period. It is noteworthy that the patient requiring the staged operative procedure had symptoms for only one day. It is probable that a primary colon resection is more feasible when the pericolic inflammatory process has had a chance to subside. Four of the five patients were aware of pneumaturia, and four also had evidence of fecaluria.

Only three of the patients gave a past history compatible with diverticulitis. The duration of their intestinal distress was 5, 13, and 17 years. Two had a definite diagnosis of diverticulitis established previously, and one of these required drainage of a peridiverticular abscess.

Abdominal examination was negative except for one man, who had a large left lower quadrant mass. This patient required the staged operative procedure.

The admitting leukocyte count was above 10,000 per cubic millimeter in two of the five patients. The urine disclosed many pus cells in all instances. Coliform bacilli and intestinal streptococci were the usual organisms found on urine culture. There was no evidence of renal insufficiency.

Excretory urography was done in four patients, without evident of renal disease. Barium enema was utilized in four cases. Midsigmoid obstruction was found in two cases and narrowing in one. Diverticula were visible in two cases, and in one of these air was seen in the urinary bladder. Cystoscopy showed localized cystitis in the four cases examined. In two of these there was definite evidence of an intestinal fistula. Proctoscopy revealed sigmoid fixation in three cases and diverticula in the fourth. However, this procedure was of value in attempting preoperatively to rule out an underlying malignant process.

Division of the sigmoidovesical connection and resection of the involved colon were carried out as a primary procedure in four cases. In one instance a staged procedure was done. There were no operative deaths. There was no evidence that the fistula increased the operative morbidity when the primary resection was employed. The staged procedure was felt to be indicated because of a large inflammatory mass adjacent to the fistula. Also, an underlying malignancy could not be ruled out.

In no instance was a definite fistulous tract visualized at operation. At evaluation of the resected colon a fistula could be demonstrated in four of the five cases. It was quite small and embedded in inflammatory tissue.

In only two of the five cases was it necessary to excise a cuff of bladder wall. As the channel is so small, it will generally require no more than division of the fistula. The area of the fistula may be ligated adjacent to the bladder. An indwelling catheter was employed for periods up to a week in the immediate postoperative period.

All of the patients were relieved of their intestinal and urinary symptoms.

Summary and Conclusions

Sigmoidovesical fistula is usually a complication of diverticulitis. A persistent lower urinary tract infection, pneumaturia, and fecaluria are the outstanding features of such a communication. Pneumaturia practically always indicates a vesicointestinal fistula. The urinary symptoms are generally more prominent than bowel distress, which may be absent. Cystoscopy usually reveals localized cystitis, and the fistula orifice may be visualized. Proctoscopy is of limited value except to exclude carcinoma. A primary colon resection and end-to-end anastomosis is feasible in many cases. A staged procedure may be necessary, depending on the condition of the patient and the extent of the inflammatory reaction. A definite fistulous tract is frequently not visualized at operation. Excision of a portion of the bladder wall may not be necessary.

Five cases of sigmoidovesical fistula secondary to diverticulitis are presented. In four instances a primary colon resection was found to be feasible. There were no operative deaths, and the morbidity was not increased.

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Abdominal Surgery in the Aged

An Analysis of Three Hundred Seven Operations

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It is apparent both from one's own experience and from population trends that the elderly patient constitutes an increasingly important segment of medical practice. This poses a challenge to the medical profession that can be met only by a thorough understanding of the problems that are peculiar to this group of patients.

In an attempt to improve our knowledge of the surgical treatment of the aged patient, a study was done of patients (65 years of age or older) who were operated on in the Confederate Memorial Medical Center from Jan. 1, 1955, through Dec. 31, 1956. These patients were from the general surgery wards alone, and a detailed study was made of those who had adbominal surgery. If a patient died while in the hospital following a surgical procedure, the death was tabulated as an operative one, regardless of the time between surgery and death.

During the two years covered by this study, there were 4508 operations performed on the general surgery service with 96 deaths, giving an operative mortality of 2.1%. During this same period there were 763 operations performed on patients 65 years and older. This series included 307 intraperitoneal operations carried out on 274 patients with 51 deaths, giving an operative mortality of 16.6%. This is the series with which the present study is primarily concerned.

The age distribution in this series showed that 135 procedures were carried out in patients in the 65- to 69-year group, 86 in the 70- to 74-year group, 41 in the 75- to 79-year group, 31 in the 80- to 84-year group, 5 in the 85- to 89-year group, and 9 in the age range of 90 years and older. The total series was almost equally divided between white and Negro patients, and there was a slight preponderance of male patients.

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Analysis of Material

An analysis of the 307 intraperitoneal procedures performed during the two-year period showed that there were 63 operations on the esophagus, stomach, and duodenum, 4 on the small intestine alone, 80 on the biliary tract, 87 on the colon and rectum, and 73 in a miscellaneous category.

Surgery of Esophagus, Stomach, and Duodenum.—An analysis of the 63 cases in this category is shown in Table 1. Of four patients who had simple closure of a gastroduodenal perforation, one died. Of 35 patients who had a subtotal gastrectomy, 6 died, and 3 of these deaths were among the 8 patients who had emergency gastric resection. These postgastrectomy fatalities included deaths from postoperative hemorrhage from an anastomotic suture line

TABLE 1.—*Surgery of Esophagus, Stomach, and Duodenum*

Operation	Emergency	Non-Emergency	Total Cases
Closure gastroduodenal perforation	4	0	4
Subtotal gastrectomy	8	27	35
Total gastrectomy	0	2	2
Gastroenterostomy	0	6	6
Gastrostomy	5	3	8
Gastrotomy; polypectomy	0	4	4
Gastrotomy; removal of phytobezoar	0	1	1
Esophagogastrostomy	0	2	2
Heller procedure	0	1	1
Total	17 (9)*	46 (5)*	63 (14)*
Mortality, %	52.9	10.8	22.2

* Figures in parentheses indicate number of deaths.

gastric malignancy), a perforated duodenal stump with peritonitis (gastric malignancy), and shock from continued bleeding from a hemorrhagic duodenal ulcer at the time of operation.

There were only two total gastrectomies, and both these patients survived. The great mortality in this category of procedures was among those patients who had gastrostomies. All patients who had an emergency gastrostomy died during their hospital stay, although several of these deaths occurred weeks and months after operation. All of these patients had insoluble disease processes, such as far-advanced head and neck malignancy or cerebrovascular accidents.

There were 14 deaths following these 63 procedures, for a mortality rate of 22.2%. This rate is divided into 52.9% for emergency procedures and 10.8% for elective surgery.

Surgery of Small Intestine.—Only four procedures were carried out on the small intestine alone (Table 2), and two of these patients died. One patient died after resection of almost all the small intestine for mesenteric thrombosis and infarction, and the other, of bronchopneumonia following resection for ileitis.

The deaths were equally divided between the emergency and nonemergency categories, and the mortality rate for all groups was 50%.

Surgery of Biliary Tract.—An analysis of the operations carried out on the biliary tract is shown in Table 3. In the group of 38 patients with cholecystectomy alone, there was one death following emergency surgery, and this was due to myocardial infarction, on the 16th postoperative day. There were 28 cholecystectomies performed in conjunction with choledochotomy, and common-duct stones were found in only 6 cases. Three deaths occurred in this group of 28 patients, and all followed elective procedures. Two of these deaths followed transduodenal exploration of the sphincter and were due to congestive heart failure and postoperative hemorrhage. A third death was due to myocardial infarction. Among 11 patients who had cholecystostomy alone, 4 died. Three of these deaths followed emergency procedures. The high mortality in this category was due to the fact that this procedure was reserved for the poor-risk patient who seemed unable to tolerate cholecystectomy.

The mortality rate for this entire category was 11.2%, while that for emergency procedures was 33.3%, as contrasted with 7.3% for nonemergency cases.

Surgery of Colon and Rectum.—Eighty-seven procedures were performed on the colon and rectum (Table 4). Three deaths were recorded in 28 patients with resections of the colon and rectum and were due, respectively, to peritonitis, unexplained hemorrhage 15 days after surgery, and cardiac failure. There were seven deaths in the patients who had cecostomy and colostomy, and six of these followed emergency procedures. Five of these patients had far-advanced malignant disease. One death followed closure of a colostomy, and there was one fatality among 23 patients who had an emergency appendectomy.

The over-all mortality in this group of patients was 14.9%, with 16.3% and 13.1%, respectively, for the emergency and nonemergency groups.

TABLE 2.—*Surgery of Small Intestine*

Operation	Emergency	Non-Emergency	Total Cases
Resection	1	2	3
Ileostomy	1	0	1
Total	2 (1)*	2 (1)*	4 (2)*
Mortality, %	50.0	50.0	50.0

* Figures in parentheses indicate number of deaths.

TABLE 3.—*Surgery of Biliary Tract*

Operation	Emergency	Non-Emergency	Total Cases
Cholecystectomy	6	32	38
Cholecystectomy with choledochotomy	0	28	28
Choledochotomy alone	0	3	3
Cholecystostomy	6	5	11
Total	12 (4)*	68 (5)*	80 (9)*
Mortality, %	33.3	7.3	11.2

* Figures in parentheses indicate number of deaths.

TABLE 4.—*Surgery of Colon and Rectum*

Operation	Emergency	Non-Emergency	Total Cases
Colon resection	3	24	27
Abdominoperineal resection	0	1	1
Colostomy or cecostomy	22	5	27
Colostomy closure	0	7	7
Colotomy for polyp	0	1	1
Closure of perforated colon	1	0	1
Appendectomy	23	0	23
Total	49 (8)*	38 (5)*	87 (13)*
Mortality, %	16.3	13.1	14.9

* Figures in parentheses indicate number of deaths.

Miscellaneous Operative Procedures.—The 73 cases included in this group are analyzed in Table 5. The greatest mortality occurred after exploratory laparotomy, when 8 of 36 patients died. Five of these patients were found to have extensive malignancies when the only procedure was local biopsy. One died in shock from intraperitoneal hemorrhage due to nonpenetrating trauma. There were three deaths among seven patients who had palliative surgery for extensive pancreatic malignancies.

The over-all mortality rate was 17.9%, while the emergency procedures carried a 25% mortality and the nonemergency ones 13.3%.

Complications and Mortality.—Nonfatal complications are tabulated in Table 6, and the three most frequent were wound infections, postoperative hypotension, and pneumonia.

There were other significant disease processes coexisting in about 33% of the elderly patients operated on, and their frequency is noted in Table 7. Arteriosclerotic heart disease and hypertensive heart disease, each with or without congestive failure, and cancer present at another site were the most commonly encountered. These disease processes did not seem to affect the mortality rate materially except for patients who were operated on with uremia, and these patients consistently had a poor prognosis.

TABLE 5.—*Miscellaneous Surgical Procedures*

Operation	Emergency	Non-Emergency	Total Cases
Hysterectomy	0	2	2
Exploratory laparotomy	18	18	36
Sliding hernia repair (abdominal approach)	1	2	
Ventral hernia repair	3	9	12
Diaphragmatic hernia repair	0	5	5
Pancreatic surgery	0	7	7
Secondary closure	4	1	5
Iliac artery graft	0	1	1
Drainage intraperitoneal abscess	2	0	2
Total	28 (7)*	45 (6)*	73 (13)*
Mortality, %	25.0	13.3	17.9

* Figures in parentheses indicate number of deaths.

The causes of death in this series are listed in Table 8. Autopsies were obtained in 21 cases, and even then the precise cause of death was not always apparent. The clinical and pathologic findings were reviewed in each case, and the most likely single cause was tabulated. There were four patients who died with peritonitis. These included a patient whose duodenal stump opened after gastrectomy and one whose duodenal ulcer reperforated two weeks after simple closure. Eight patients had pneumonia or pulmonary congestion at the time of their death, and no better cause for their death could be found. Both patients whose deaths were caused by pulmonary embolism had confirmatory post-

TABLE 6.—*Nonfatal Complications*

Complication	No. of Patients
Wound infection	22
Severe hypotension	14
Pneumonia	10
Cardiac failure	6
Cardiac arrhythmias (new)	6
Urinary tract infection	6
Thrombophlebitis	4
Peritonitis	3
Intestinal obstruction	3
Wound hemorrhage	3

TABLE 7.—*Coexisting Diseases*

Disease	No. of Patients
Arteriosclerotic heart disease	42
Hypertensive cardiovascular disease	39
Congestive heart failure	36
Cancer of another site	23
Chronic renal disease	20
Benign prostatic hypertrophy	17
Chronic pulmonary disease	15
Diabetes	14
Previous cerebrovascular accident	10

TABLE 8.—*Fatal Complications*

Cause of Death	No. of Patients
Heart disease	9
Pneumonia	8
Shock	8
Uremia	6
Metabolic	6
Undetermined	5
Peritonitis	4
Pulmonary embolus	2
Cerebrovascular accident	2
Intestinal obstruction	1
Total	51

mortem examinations. Of nine patients listed as having cardiac deaths, three had coronary thrombosis, five had severe cardiac decompensation with arrhythmias, and one had a cardiac arrest during anesthesia. Six patients were included in the metabolic group. These were patients who had extensive malignancies and debilitation, and no other cause for death was found. Eight patients died in shock, including four who bled postoperatively, one who had uncontrolled hemorrhage during surgery, one who died after extensive resection for mesenteric thrombosis, and two whose shock was unexplained. Six patients died with uremia, and two of these had marked uremia at the time of surgery. The patient who died of intestinal obstruction developed this after partial dehiscence of small bowel around a new colostomy which had been done for benign disease.

Of the patients who succumbed, 27 were operated on as an emergency, and 21 of the 51 patients were operated on for malignant disease.

Sixteen patients died during the first 3 postoperative days, and 13 of these died during the first 48 hours. A list of the postoperative days of death for the entire series follows: day of surgery, 6 cases; 1st postoperative day, 7 cases; 2d day, 1 case; 3d day, 2 cases; 4th to 6th day, 8 cases; 7th to 13th day, 10 cases; 14th to 20th day, 10 cases; 21st to 29th day, 1 case, and 30th day and later, 5 cases.

Comment

The over-all operative mortality in this series of abdominal operations in patients 65 years or older was 16.6%, and this is considerably higher than the 2.1% mortality rate for all operations on the general surgery service during the same period. The rate for nonemergency surgery was 11.1%, as compared with 26.8% for emergency procedures. Although it is difficult to compare these results with others reported in the literature because of many variables, these rates appear somewhat higher than those reviewed. Anglem and Bradford [1] reported 443 abdominal operations in patients over 70 years of age, with an elective mortality of 10.1%, an emergency mortality of 19.2%, and an over-all mortality of 11.5%. Haug and Dale [3] reported 354 surgical procedures in patients over 60, with an elective mortality rate of 5.7%, an emergency rate of 21.9%, and an over-all mortality rate of 9%. Welch [4] reported 140 abdominal operations in patients over 70, with an elective mortality rate of 13.8%, an emergency mortality rate of 39%, an over-all mortality rate of 20.7%. Gilchrist and de Peyster [2] reported mortality rates for 223 major abdominal procedures in patients over 70 years of age to be 7.6% for nonemergency cases, 23.1% for emergency cases, and 9.4% for all cases. Any attempt to explain discrepancies in mortality rates of different series is pure speculation, but it should be noted that all patients in our series were ward patients, many of whom suffered from marked deficiency states.

The effect of increasing age on surgical mortality is clearly shown by analysis of this series. The mortality rate for operations on patients between 65 and 75 years of age was 13.5%, and this increased to 23.1% for patients over 75.

While coexisting disease in itself usually did not affect the mortality, the presence of uremia at the time of surgery was of ominous prognostic significance. The finding of azotemia should be evaluated carefully, for the outlook in the patient with increasing values for blood creatinine and urea nitrogen, in spite of adequate therapy,

is indeed poor. It is doubtful whether any but obvious life-saving surgery is indicated in such a case.

An analysis of the fatalities in this series of abdominal operations helps to clarify the pitfalls of surgery in this age group. About one-fifth of the deaths were due to some complication of the initial surgical disease, such as reperforation of a perforated duodenal ulcer after closure or exsanguinating hemorrhage from a hemorrhagic duodenal ulcer during surgery. Only about one-seventh of the group died of a complication of the surgical procedure itself. One-fifth of the deaths were of patients whose condition was such that they did not tolerate the surgical procedure, regardless of its magnitude; included in this latter group are those patients who died after exploratory laparotomy and in whom little or no cause for death was found. Almost one-half of the total fatalities were caused by complications which were unrelated to the surgical disease.

It becomes apparent from a study of this type that many patients in this older age group have poor physical reserve, even though they appear to be fair to good risks. This lack of reserve seems to contribute considerably to their morbidity and mortality. This finding is best reflected in the manner in which patients recover from their postoperative complications. Not only do minor complications seem to become major hazards but frequently one minor complication follows another, and the summation of these seems to exhaust the patient. Whereas a younger patient can withstand the prolonged morbidity, the older patient may succumb.

The contrast of the nonemergency mortality rate of 11.1% and the emergency mortality rate of 26.8% is the most significant finding in this study. This disparity was noted in every category of surgical procedure carried out in the elderly patient. It varied from 1:5 for the upper gastrointestinal surgery to 1:1.2 for the colon surgery. A similar disproportion between emergency and elective mortality rates have been reported by others,[1-4] but its importance seems worth emphasizing. It should prompt one to postpone surgery in the elderly patient until he is in optimal condition and to avoid emergency surgical procedures when possible. This indicates that elective surgery, with its lower mortality rate, may be justified in persons of this age group for correction of hernias, removal of gallstones, etc., to rid them of potential causes for emergency procedures. Certainly it places considerable responsibility on the physician who advises a patient not to have an operation because of advanced age.

It is doubtful that mortality rates in patients over 65 years of age will ever be as favorable as those in the younger group. However, most surgeons agree that there are certain factors of major importance if the mortality is to be minimal. These factors include restoration or maintenance of a normal blood volume, avoidance of infection, judicious use of antibiotics, control of fluids and electrolytes, and careful evaluation of coexisting disease. Attention to these details will allow one to perform surgery in the aged with optimism and enthusiasm. Only with such a sound physiologic approach can one truly believe that age is no contraindication to surgery.

Summary

A study is presented of 307 intraperitoneal operations performed on 274 patients who were 65 years of age or older. These procedures were divided into categories according to anatomic site, and each category is analyzed for factors affecting mortality.

There were 51 deaths in this series, an operative mortality of 16.6%. This is considerably higher than the 2.1% mortality rate for all operations on the general surgery service.

An analysis of the complications shows that the three most frequent nonfatal complications were wound infections, postoperative hypotension, and pneumonia.

Other significant disease processes were present in about one-third of the elderly patients. The commonest of these was heart disease, but none of these diseases affected the mortality rate except the presence of uremia, which consistently signified a poor prognosis.

A review of the deaths in this series revealed that approximately one-third occurred during the first three postoperative days. The commonest causes of death were heart disease, pneumonia, and shock. About one-half of the total fatalities were caused by complications unrelated to the surgical disease.

The increased hazard of emergency surgery in the elderly patient is clearly illustrated by a mortality rate of 26.8%, as contrasted with a rate of 11.1% for nonemergency procedures.

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Advances in Abdominal Surgery

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In discussing advances in abdominal surgery, I have chosen to limit my remarks to progress made during the last 16 years, beginning with the American entry into World War II, in December, 1941. My personal acquaintance with surgery dates back almost 40 years, after graduation from Rush Medical College of the University of Chicago in April, 1919. It seems to me that the most rapid, exciting, and valuable advances in surgery have taken place in the past 16 years. There were many important contributions which made these advances possible; for the sake of brevity, I shall only enumerate them. They were the discovery of the sulfonamides, the antibiotics, the extended application of the giving of blood, the maintenance of proper fluid and electrolyte balance by intravenous injection of replacement agents, and the use of gastric and intestinal intubation with suction by means of catheters and the Miller-Abbott tube. As newer surgical techniques were introduced, it followed that new instruments were needed, and these were developed. Improved and better-controlled anesthesia, including hypothermia, similarly contributed to the reduction of operative risks, making it possible to do operations hitherto thought impossible, with survival of the patient. Many of the physiological, chemical, and anatomical studies which were the basis of these developments were first carried out in the experimental laboratory, before the procedures based on them were applied clinically.

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In 1915, in discussing arteriovenous aneurysms, Osler [1] commented:

> It is not too strong a statement to make that up-to-date vascular surgery cannot be done in a hospital whose younger surgeons have not full opportunities to experiment upon animals. The extraordinarily delicate technique of vascular suturing is an art acquired only with much practice.

How completely Osler's ideas have been followed in the opportunities provided, not only for young surgeons but for the training of interns, residents, and fellows, and not only in the field of vascular surgery but in all other surgical fields as well! This particular type of training has been one of the most important factors in elevating American surgery to its present high position, and it accounts for many of the advances which have taken place in all fields of surgery. Actually, in recent years, while listening to some of the papers presented before some of our leading surgical societies, I have wondered whether or not I might be attending a meeting of physiologists or biochemists—and so I was, but they were surgeons also, applying the basic principles of these and others of the basic sciences to problems occurring in their patients, and conquering them.

For the most part, I am going to discuss the advances made in the treatment of abdominal visceral lesions, including, however, the adrenal glands and the aorta and its main branches. The better to do this, I have chosen first to comment on the advances made in vascular surgery to show how these advances came about, not alone because they have been among the most spectacular and valuable but because they illustrate the processes of surgical progress.

To return to Osler's paper*: In giving a brief history of the development of vascular surgery, he spoke of the rarity of arteriovenous aneurysms at that time, both in Canada and in England. He said that the Museum of the Royal College of Surgeons of England had only three specimens of such a vascular process.

He commented thus:

A new and truly marvellous technique has been developed in vascular surgery, very largely owing to the work of Alexis Carrel, and [note this, please] the increasingly favorable results in this all-important department of surgery have followed directly upon animal experimentation. . . . Within the next year there will be greater opportunities for vascular surgery than have ever before been offered. The results of the last wars should be carefully studied by our surgeons.

These principles of development can be said to have applied to almost every field of surgery during and subsequent to World War II, augmented by results learned from the treatment of the wounded in the Korean conflict and the development of techniques based on sound physiological principles.

Two days before Christmas I repaired a large postoperative hernia in a patient's anterior abdominal wall. This fault had developed after successful resection of an abdominal aneurysm and the insertion of a homologous arterial graft 10 months previously elsewhere. Before the hernia was repaired, thorough abdominal exploration was made. When the abdominal aorta was palpated, it would have been impossible to ascertain that a graft had been inserted had it not been for a ring-like thickening at the ends of the graft. Pulsation throughout the palpated segment was normal; it had not dilated, and there was no reaction around the engrafted portion. A perfectly marvelous achievement!

* Osler attributed to Rufus of Ephesus (Greece) and Antyllus (Greece) the first reported work in vascular surgery and described Antyllus' method of surgically treating aneurysms.

Vascular Anastomoses and Transplants

My colleague Dr. Joseph M. Janes,† who, prior to coming to the Mayo Clinic in 1938, and for a short time after, had worked with Gordon Murray of Toronto, in his experiments with heparin and the use of vein grafts, tells me that, although many advances were made in vascular surgery during World War II, it was the Korean conflict which gave the greatest impetus to the use of vascular anastomoses. Vascular grafting for early definitive surgical treatment became possible, viable fresh grafts were readily obtained, and blood was available for replacement. About this time Blakemore [2] and Hufnagel [3] were studying experimentally the results of bridging the defects in blood vessels by the use of such prosthetic links as Vitallium and polyethylene tubes, and later my colleagues Mortensen and Grindlay [4] began to use polyvinyl formalinized sponge (Ivalon sponge) compressed into a tubular form in experimental animals. It was Gross,[5] however, operating upon several patients with coarctation of the thoracic aorta, who excised the constricted area and inserted a vascular graft. This gave great impetus to the clinical application of vascular grafting. In his book on plastic arterial grafts, Edwards [6] wrote that Gross' contribution "stimulated a renewed investigation of techniques of arterial transplantation and led to the development of a technique of short term preservation of living homologous arterial grafts in 10% homologous serum in a balanced salt solution."

In 1951 Marrangoni and Cecchini [7] and Natellis and Visalli [8] made more practical the development of arterial homograft banks by their introduction of a method of freeze-drying homografts to preserve them. I do not know how many grafts of this type have been inserted into the aorta to replace

† During World War II Dr. Janes was attached to the Medical Corps of the Royal Air Force and successfully applied many of the lessons learned in his experimental work to vascular surgical problems in the wounded.

abdominal aneurysms, but I am sure it is many hundreds. Many more have been used in the treatment of the Leriche syndrome, resulting from occlusive disease of the iliac arteries. Great credit is due to De Bakey, Cooley, and Creech,[9] at Baylor, for showing how successfully such operations can be performed.

Most of the grafting operations have been successful, but some have failed because of weakness of the transplant at the site of a ligated branch vessel. Recently, more and more applications have been found for the synthetic-material tubular graft because of the availability and strength of this material. W. Sterling Edwards, working with Dr. James Tapp and Mr. Pat Moore, devised a crimp tube of braided nylon (treated with formic acid), which can be bent without kinking and which has served very well as a vascular graft in the hands of our vascular surgeons and others, and has practically replaced the homograft in some areas.

The application of vascular anastomosis is noteworthy in the splenorenal shunts and the portacaval anastomoses done for bleeding esophageal varices.

Although it had been suspected for a long time that portal venous pressure might be increased in patients who had splenomegaly and bleeding from esophageal varices, it remained for the group headed by Whipple to establish this point in 1936 and in 1937 by direct measurement of such at laparotomy. Out of such early work have grown the surgical procedures [described].[10]

The foregoing was the introduction of my colleague, Dr. George A. Hallenbeck, to the report in 1955 on the results of portacaval anastomosis. In a later report, in July, 1957,[11] he analyzed 55 cases.

He said that in selecting patients for operation he uses the criteria presented by Linton and Blakemore, and that the evidence indicates that, although large, well-placed portacaval or splenorenal anastomoses do not provide absolute protection against subsequent gastrointestinal bleeding, they are effective in most instances. In addition to these procedures, the transesophageal ligation of varices is being done in children.

Time does not permit a continuation of the discussion of other developments in this fascinating field of endeavor if we are also to consider other noteworthy, but less spectacular, achievements in abdominal surgery.

Hyperfunctioning Adrenal Lesions, Cortical and Medullary

To me one of the most interesting accomplishments in abdominal surgery has been the recognition and treatment of hyperfunctioning tumors of the ductless glands. I refer particularly to the hyperfunctioning insulinomas of the pancreas, which produce the Whipple triad ‡ of symptoms and hyperfunctioning tumors of the adrenal cortex and the adrenal medulla.

My interest in adrenal lesions was aroused in 1923, when I [12] was an assistant to the late Charles H. Mayo. We operated upon a patient who had extremely high blood pressure, which was particularly increased when anything was done that increased her pulse rate, such as strenuous exercise and frequent body bending and during periods of stress. The diagnosis was obscure, but it seemed as if a tumor was palpable in the upper left part of the abdomen, and abdominal surgical exploration was advised. This led to the finding of a left adrenal medullary tumor, at that time called "paraganglioma," and now "pheochromocytoma." When this adrenal tumor was removed, the patient's blood pressure returned to normal, and an uneventful convalescence followed.

At about this time I assisted "Dr. Charlie" in removing from another patient a large malignant tumor also involving the left adrenal body.[13] The malignant cells were cortical, for the most part. Apparently they were in a much greater hyperfunctioning state than we suspected, and the patient's postoperative course was characterized by an

‡ Whipple triad of symptoms: intermittent episodes of hypoglycemia (less than 40 mg. per 100 cc.) associated (1) with neurologic symptoms, which are relieved by injections of dextrose, and (2) with reproduction of the syndrome by fasting.

increase in respiratory rate, temperature, and pulse rate, and a decrease in blood pressure and output of urine, obviously due to adrenal cortical insufficiency. Although the usual methods of therapy of that time were employed, the patient died. At postmortem examination an atrophic adrenal gland was found on the opposite side.

This experience led to the recognition that when one adrenal gland is overfunctioning, temporary hypofunction with hypoplasia of the opposite gland requires adrenal substitutes, or their chemical equivalents, which are necessary to prolong life until the hypoplastic adrenal gland becomes active. Later, Kepler, Wilder, and I [14,15] reported a series of adrenal cortical tumors which I successfully removed after the patients had been prepared for operation by the use of adrenal cortical substances, which our colleague, Kendall, prepared for us. When Kendall isolated cortisone and hydrocortisone from the adrenal bodies of animals, for which feat he shared the Nobel Prize in 1950, we used these steroid compounds in preparing for operation patients with hyperfunctioning adrenal cortical tumors and patients for whom adrenalectomy was to be done. After Kepler and Wilder, and later Sprague and his associates, began to prepare these patients for operation with Kendall's adrenal extracts and with plenty of sodium chloride and sodium citrate, and later with cortisone and hydrocortisone, I cannot recall the loss of a single patient from whom a hyperfunctioning adrenal cortical tumor was removed. This replacement therapy enabled my colleagues, Sprague and Priestley, and me to carry out at first extensive subtotal adrenalectomy in the treatment of Cushing's syndrome,[16] and to use total adrenalectomy [17] when the condition was more serious, with a minimum mortality rate and with amazingly good results.

To see the change occurring in these patients before and after operation is remarkable. The reduction in the hypertension, the loss of the buffalo-like type of obesity, the clearing of the acneiform eruptions, the disappearance of hirsutism from the face and chest of women, and the return of the menstrual cycle in women are objective indications of the accomplishments of surgery in this instance. We used to do the operation in two stages, with a time interval between. Now it is done as a one-stage procedure. Here the reduction of mortality has been due to the application of the principles of physiological adrenal cortical replacements. The administration of these agents prior to operation to form an intramuscular deposit of cortisone, with continuation of their use, as needed, after the removal of hyperfunctioning tissue, is essential.

The continuous use of cortisone or other adrenal steroids in the treatment of the pain of arthritis and other collagen diseases produces hypofunctioning of the adrenal glands and increases the risk of postoperative shock, and even death, after any operation unless these possibilities are recognized. Preparation with cortisone should be carried out by the intramuscular administration of 200 mm. of cortisone for two days prior to operation, and administration should be continued as needed afterward. If shock should occur in patients who have not had the aforementioned depot of cortisone injected prior to operation, the intravenous administration of hydrocortisone will be found very valuable.

In 1954, and in 1956, Conn,[18,19] of the University of Michigan, described cases in which primary aldosteronism was caused by adrenal cortical tumors. The major clinical manifestations of the syndrome consist of periodic attacks of severe muscular weakness associated with marked hypokalemia, intermittent tetany and paresthesia, polyuria and polydipsia, hypertension, and hypernatremia and alkalosis. Edema is noted. Values for hydrocortisone (17-hydroxycorticosterone) and 17-ketosteroids were consistently normal, contrary to the situation in Cushing's syndrome, in which values for one or both are consistently elevated and an increased amount of aldosterone is excreted.

In his 1956 report, Conn collected and reported 12 cases of primary aldosteronism, in all of which an adrenal cortical tumor was found either at operation or at necropsy. Nine patients had been relieved of their symptoms by surgical removal of the adrenal gland (in the other three the lesions were recognized in retrospect at necropsy). It was Conn's belief that in some patients adrenal adenomas will not be found, for in one case in his series no adrenal tumor was found at necropsy. He wrote that in these cases extensive subtotal or total adrenalectomy should be done. One patient was reported to have been cured by bilateral adrenalectomy.

I have successfully removed aldosterone-producing adrenal tumors from three such patients during the past year, with the anticipated relief of symptoms.

On the same day that I operated upon the patient with the ventral hernia for whom aortic transplantation previously had been done, a telephone message from a surgical friend asked me to see a patient whom my colleague, Dr. John M. Waugh, had operated upon that morning. He had removed a very large (13×11×11 cm.) pheochromocytoma which had destroyed the left adrenal gland. Dr. Grace M. Roth, who has established a national reputation for her physiologic studies of peripheral vascular diseases,[20] and who has devised tests for determining the presence of pheochromocytomas, told me that this patient had more pressor amines circulating in the blood stream (more than 90μg.) than any of the other 57 whom she had studied.[21] In preparing the patient for operation and taking her to the operating room, and during the operation and subsequently, Dr. Roth and her medical associate were administering phentolamine (Regitine) to reduce the blood pressure when necessary and arterenol to increase it as indicated. With such control of blood pressure available, the patient's blood pressure became stabilized at a normal level three hours after the operation. She appeared to be well, with a normal blood pressure, the next morning, and convalescence was uncomplicated.

There have been no deaths among the 58 patients operated upon at the Mayo Clinic for pheochromocytoma. This over-all result can be attributed to the teamwork of the clinician, the physiologist, the surgeon and his assistants, and the anesthetist, particularly by satisfactory control of the varying blood pressure.

Pancreatic Insulinomas and Biliary Stricture

Hyperfunctioning tumors of the islands of Langerhans which produce hypoglycemia, resulting in the Whipple triad of symptoms, have been recognized as an entity since the time W. J. Mayo found such a malignant tumor of the pancreas which had metastasized to the liver. Wilder, Allan, Power, and Robertson[22] were able to isolate insulin from the metastatic tumor in the liver. Later, Whipple described the clinical syndrome associated with the hyperfunctioning tumor of the islands of Langerhans, and in 1950 Howard, Moss, and Rhoads[23] presented a comprehensive review of hyperinsulinism and islet-cell tumors of the pancreas and collected 398 tumors, 224 of which were removed at operation. It must be remembered, as these authors pointed out, that some of these tumors are multiple and that most of them are present in the body and the tail of the pancreas and are removable by local excision, or, when they cannot be palpated, by subtotal pancreatectomy. In some cases, however, the tumor is situated in the head of the pancreas where, if the lesion is not palpable, radical resection of the duodenum with the remaining part of the pancreas and the lower part of the common bile duct may be required, with restoration of gastrointestinal-pancreatic-biliary continuity. This is a formidable procedure.

However, it may be possible to remove the insulinoma by segmental resection of that portion of the pancreas which lies above the duodenum and above the pancreatic por-

tion of the common bile duct. I recently operated upon a patient in whom this was possible. Fortunately, the hyperfunctioning adenoma was 2 cm. in diameter and thus could be palpated.

The corollary of this is that if the patient has the Whipple triad and an adenoma is not palpated in the pancreas, the tail and the body of that structure should be removed. Removal in this instance can be accomplished best by removal of the spleen with the tail and body of the pancreas. If, after multiple sections of the removed portions of the pancreas do not reveal a hyperfunctioning islet-cell tumor and the patient continues to exhibit symptoms, it will be necessary to perform radical pancreaticoduodenal resection at a later time. At that time, however, the possibility should be borne in mind that supraduodenal partial resection may reveal the tumor.

Three and a third years ago I operated upon a patient for whom total pancreatectomy had been performed in stages because symptoms of hypoglycemia had persisted after initial resection for a malignant insulinoma. I removed a metastatic carcinoma 2.5 cm. in diameter from the right lobe of this patient's liver, and this operation provided relief of his symptoms of severe paroxysmal hypoglycemia for more than a year. Later these symptoms again appeared. The patient was referred to his original surgeon, who lived close by and who successfully removed three other metastatic tumors from the left lobe of the liver. At the time of this report the patient had continued to be well.

Radical resection of the head of the pancreas and of the duodenum and the lower part of the common bile duct continues to be the best procedure for carcinoma of the lower part of the common bile duct and the ampulla and papilla of Vater. In a study of 85 radical pancreaticoduodenectomies performed at the Mayo Clinic up to Jan. 1, 1953, Waugh and Giberson [24] reported that 5 of 13 traced patients (38.4%) with ampullary carcinomas survived the operation five years or more, whereas when the same radical procedure had been performed for carcinoma of the head of the pancreas only 3 of 19 traced patients (15.8%) survived five years or more. The important point here is that radical resection for ampullary lesions has justified itself even beyond expectations, and if the lesion in the head of the pancreas has not become fixed to surrounding structures, making complete removal of it impossible, radical resection is a worthwhile procedure. When the pancreatic tumor has become fixed and inoperable by its invasion of arteries and veins, biliary intestinal anastomosis will relieve the patient's jaundice, and gastroenterostomy will relieve duodenal obstruction (if it is present) and may prolong the patient's life for about a year.

Now what of the surgical treatment of chronic recurring pancreatitis? The problem here is to distinguish between the interstitial type unassociated with obstruction of the pancreatic duct and that type in which distal obstruction of the pancreatic duct has occurred, with distention of the duct system. If pancreatic stones are obstructing the duct, they should be removed. If the obstruction is inflammatory, amputation of the tail of the pancreas and performance of pancreaticojejunostomy, usually by the Roux-Y procedure, have given good results in many cases in which other, more conservative methods have failed. By "more conservative methods" I mean prolonged T-tube drainage of the common bile duct or choledochoduodenostomy or sphincterotomy (cholecystectomy should be a part of these procedures). My experience with sphincterotomy in these cases has not been very satisfactory, nor has the operation of choledochoduodenostomy. I have performed these operations both separately and in combination when symptoms have been unrelieved by one or the other of the two procedures. Yet the best I have been able to accomplish is relief of symptoms in about 65% of cases, and in some of these the symptoms were not completely relieved.

Moreover, sphincterotomy in particular is accompanied by a more than average operative risk because of the possibility that acute hemorrhagic pancreatitis may develop after the operation.

In two patients for whom I performed sphincterotomy spasm of the wall of the duct and a reproduction of the clinical symptoms occurred after the injection of a radiopaque substance (25% thorium dioxide; Umbrathor) into the duct. (One of the patients was allergic to iodine, and so the solution of thorium was used.) Spasm increased the intraductal pressure tenfold (more than 300 mm. of water), and in one case the thorium was seen roentgenologically to enter the pancreatic duct. Two long hypodermic needles placed in the lumbar ganglion and injection of procaine hydrochloride immediately relieved the pain, although the high intraductal pressure and distention of the common duct caused by ductal spasm persisted. This ductal spasm probably explains the symptoms which continue after sphincterotomy and indicates the advantages of a therapeutic block with procaine hydrochloride, which, if successful, can be followed with the injection of a very small amount of absolute alcohol.

In two patients operated upon elsewhere almost complete obstruction occurred postoperatively at the site of a previously performed sphincterotomy. In one of these (a patient operated upon elsewhere) a long T-tube of small diameter had been used, but it was inadvertently pulled out only eight days postoperatively. Evidences of biliary obstruction developed a few weeks later.

Interest in the treatment of stricture of the common bile duct was stimulated by the anticipated and unpreventable news items concerning surgical correction of this condition in the United States in an internationally known statesman of another country. In my experience in correcting this serious condition in more than 365 patients operated upon since 1924, I have found that most such strictures resulted when, for one reason or another, the surgeon did not identify the common bile duct and the common hepatic duct, and separate the cystic duct and artery from them before they were divided. I am very charitable in discussing strictures of the common bile duct because about 25 years ago I cut the common bile duct in two cases—restoring continuity immediately in one and not until five days later in the other—both patients, fortunately, had no untoward results.

My best results have followed anastomosis of the duct, above the site of stricture, to the duodenum, although in the smaller number of patients who had a short stricture that could be excised and an end-to-end anastomosis made, the results have been just about as good. Similarly, Aust and Varco [25] found the results of biliary-duodenal anastomosis to be superior to the results of biliary-jejunal anastomosis. The results have been excellent or good in about 75% of cases. If symptoms of cholangitis develop postoperatively—and they may arise as late as 10 or 15 years later—the cholangitis is always on an obstructive basis at the site of anastomosis and is not regurgitant.

Peptic Ulceration and Nonspecific Islet (Langerhans)-Cell Tumor

At the 1955 meeting of the American Surgical Association here in Philadelphia, Zollinger and Ellison [26] reported three cases of recurring jejunal ulceration in which nonspecific islet-cell tumors of the pancreas eventually were found. All three patients had marked hypersecretion and hyperacidity. The authors reported four additional cases from the literature. A more recent paper by Ellison reports more than 20 cases.[27] The chief import of these studies, in respect both to recurring peptic ulceration and to nonspecific islet-cell tumors in association with such ulceration, is that when peptic ulceration recurs the surgeon should carefully search the pancreas for palpable adenomas and remove them at the time of the surgical procedure performed for the recurring ulceration. Unfortunately,

in most cases, the tumors have been small and thus escaped detection; sometimes they were multiple, and frequently they were malignant.

I have not encountered any instances of recurring ulceration and associated pancreatic islet-cell adenoma. Actually, when large recurring gastrojejunal ulcers were encountered in which the anastomosis had been made posterior to the colon, the penetration of the ulcer to the capsule of the pancreas and the contiguous inflammation and induration which had developed made it impossible for me to determine that such a tumor was not present, and yet recurring ulceration has not developed among such patients with the frequency of the ulceration reported among patients with pancreatic lesions.

At the last meeting of the Interstate Postgraduate Medical Association of North America, my surgical colleague, Dr. George A. Hallenbeck, and I were given four cases to present and discuss. One of the patients was a middle-aged woman who had undergone a Billroth I gastric resection for a perforated gastrojejunal ulcer which had produced a gastrojejunocolic fistula after gastroenterostomy done for duodenal ulcer. Vagotomy also was done. You will recall that the Billroth I type of gastric resection restores continuity by joining the proximal end of the resected stomach to the duodenum, in contrast to the Billroth II resection, in which the resected stomach is anastomosed to the jejunum. Last year my assistant, Dr. T. E. Lynn, and I [28] reported on a 5-to-10-year follow-up study of patients with duodenal, gastrojejunal, and gastric ulcers for whom the Billroth I and Billroth II types of resection had been performed. It was found that the incidence of recurring ulcer in cases of duodenal ulcer and of gastrojejunal ulcer after the Billroth I operation was two to three times that which followed the Billroth II procedure. Therefore, I was not greatly surprised to hear that the patient being presented had had an intestinal hemorrhage not long after performance of the Billroth I resection (even with vagotomy added), and the crater of a recurring duodenal ulcer was demonstrated roentgenographically. The patient's surgeon did another resection of the stomach and converted the Billroth I anastomosis to a Billroth II procedure and also performed vagotomy. Exploring the pancreas, he found a nonspecific islet-cell adenoma, which he removed. The patient had been well since that time, but only a few months had passed since the operation at the time we saw her. Vagotomy has a useful place in the treatment of recurring ulcer after adequate resection and in some cases when gastrectomy cannot be performed safely if gastroenterostomy is done at the same time.

Use of Segments of Intestine as Conduits and Containers

A discussion of intra-abdominal surgical advances would not be complete without some attention to the very satisfactory results which have followed the use of segments of small intestine to replace segments of ureter, or to add to the capacity of a contracted bladder as a reservoir for the accumulation of urine, or to replace a bladder with ureters transplanted into the new structure. The advantages of emplacement of such a segment of small intestine in the urinary tract without absorption of urine, to the detriment of the patient, have added to the scope of operations on the urinary tract and to those "All-American" operations of removal of uterus, tubes and ovaries, rectum, bladder, and the iliac lymph nodes in the treatment of extensive recurring malignant lesions of these structures, particularly the cervix and uterus. Segments of both small and large intestine have been interposed between the stomach and the duodenum in cases in which the Billroth I type of gastric resection has been used for duodenal ulcer to increase the food capacity of the gastric segment.

Unfortunately, these new procedures have been followed by the same incidence

of recurring ulceration (8%) as follows the Billroth I operation without the intestinal transplant. For a short follow-up period of less than two years the transplant operation seemed to have merit and to permit a better nutritional status and a gain in weight, with a lower incidence of the dumping syndrome. Still, a year later recurrences of the duodenal ulcer had manifested themselves.

This prolongation of a period of postoperative studies is one of the most important factors to be considered in evaluating new or modified surgical procedures, especially in the treatment of peptic ulcerations. Variable periods of follow-up study probably constitute an important reason for the differing results which follow the same type of operation performed by different surgeons.

Operations for Malignant Disease

Since it is now possible to perform more radical operations with increased safety, the question naturally follows why, if recurrence takes place in that part of the stomach remaining after subtotal gastrectomy for malignant lesions (as in my experience it does not), total gastrectomy rather than subtotal gastrectomy should not be carried out. Hence such a course actually was pursued for a time by Lahey and Marshall. They found, however, that the survival rate was not lengthened thereby, the postoperative functional result was not nearly so good, and the mortality rate was increased as compared with those factors after subtotal gastrectomy. They therefore returned to subtotal gastrectomy when total gastrectomy was not actually a necessity.

My colleagues and I [29] have used total gastrectomy only when it has had to be done, and when subtotal removal would not be adequate for removal of the malignant process and tissues for 4 cm. beyond. However, in the past few years the number of total gastrectomies performed in proportion to the number of subtotal gastrectomies carried out has increased, averaging from about 27, for total gastrectomy, to about 180, for subtotal gastrectomy per year.

Recently, at the Southern Surgical Association, Fly, Priestley, Comfort, and Gage [30] presented a study of 150 total gastrectomies performed during the period of 1917 through 1954 at the Mayo Clinic for patients who survived five years or more. There was a five-year survival rate of 12%. In 51 of the cases there was no metastasis, and in these the survival rate for five years or more was 21.6%. This increase in the number of resections of the stomach also was noted in the case of subtotal gastrectomy, in which a reduction in the mortality rate took place and in which the five-year-survival rate increased 180% [31] during our 1940-1950 period, as compared with our earlier period.[32]

An increasing number of partial hepatectomies is being reported each year. The risk of the operation is not excessive, and the operative procedure is not difficult. It has been done in cases of unilobar hepatomas and in some malignant lesions, both primary and metastatic; but it is, as might be expected in metastatic lesions, a palliative procedure.

Surgery of the colon for malignant disease has been greatly changed as a result of the preoperative use of the broad-spectrum antibiotic agents combined with complete emptying of the intestine and colon of fecal material and barium by the use of saline cathartics and colonic irrigations. When the bowel is empty, and intestinal secretions are reduced and the amount of bacterial flora is decreased to a minimum, one-stage operations without colostomy now are the rule rather than the exception. In such instances the risk of operation has been reduced to that of resection of the upper part of the gastrointestinal tract, with the benefit of a shortened convalescence, an earlier return to work, and a marked lowering of hospital expenses.

More rectal-sphincter-preserving operations have been done, with results seem-

ingly as good as those of radical abdominoperineal resection, if the lesion is situated high enough in the rectum to permit the sphincter-preserving operation. Swenson's contribution to knowledge of the causes of Hirschsprung's disease in children, and the removal of the aganglionic segments of the sigmoid and the pulling through the dilated anus of the rectosigmoid, with anastomosis of the ends from the perineum, have constituted a great advance in the treatment of this disease. This type of operation also has been applied to low, localized rectal lesions of a low grade of malignancy.

In all gastrointestinal operative procedures the postoperative use of the indwelling nasal gastric suction catheter, as described by Wangensteen, has given comfort to the patient, has reduced intestinal distention to a minimum, and has helped to reduce the operative risk by preventing gaseous pressure at the site of the anastomosis. The use of this measure in the period of preparation of patients with gastrointestinal obstruction has emptied the gastrointestinal tract of secretions and gas. When the measure has been combined with the other methods of restoring fluid and electrolyte balance and plasma protein levels, it has lessened the hazards of the operation and made it less difficult to perform.

In a symposium on new operations appearing in the *Surgical Clinics of North America*, Cole,[33] the consulting editor, in a foreword, wrote as follows:

> It is my belief that the reader will find in these pages a vast amount of useful information. There can, however, be no guarantee that all of these operations will survive the passage of time; some inevitably will be replaced by newer and still better procedures. It is well known that progress can be made only by the process of substitution of one technique for another.

This reasoning is sound, and the average surgeon will heed the implied comment that until time has shown one procedure to have greater value than another, it is best to continue with the time-proved procedure which has given the best results. It must be remembered that in making progress there are enthusiasts who may extend the indications for operation beyond a point advantageous to the patient. This means that surgical procedures may be so extensive, without hope of cure, that the patient never quite recovers or, if he does, he is not well. In fact, the patient may be miserable and the expense of a prolonged, complicated postoperative course may expend his small life savings, so that when he dies his family is left but little means to carry them through the period of adjustment. This should not be.

Miscellaneous Procedures and Measures

Hand in hand with the untoward philosophy just mentioned is the thesis that extensive and repeated laboratory procedures should be done routinely for every patient. These are expensive for the patient and add an unnecessary load to our overworked laboratory colleagues and their assistants. I should like to mention one example, which gives me a chance to compliment the chemists and the radiologists who have made it possible to visualize the common bile duct by the intravenous injection of the concentrated iodine solution iodipamide sodium (Biligrafin; Cholografin). This radiologic examination, when results are positive, is worth the expense; but when the history and the physical findings point to repeated obstruction of the common bile duct for which abdominal exploration and exploration of the common duct and pancreas must be done, I think the roentgenologic test is seldom indicated. If the result of the roentgenologic test is negative, surgical exploration will have to be done anyway.

Another example is the routine use of the complete battery of tests of hepatic function, so frequently regarded as a necessity in spite of the fact that the patient has clinical evidence of obstructive jaundice. In most cases but two or three tests are necessary, and these should be employed to determine hepatic function rather than as differential diagnostic tests. Seldom is

it necessary to repeat such tests postoperatively if everything possible has been done to relieve the biliary obstruction and if postoperative care has been of the proper quality, especially if the patient's progress is satisfactory.

The widespread use of chlorpromazine hydrochloride (Thorazine) as a tranquilizing agent can implant a diagnostic problem in patients with jaundice, in whom an intrahepatic cholangitic accumulation of bile-pigment sediment may develop, producing intrahepatic obstructive jaundice. This may be difficult to distinguish from extrahepatic jaundice—and, of course, a patient who has taken chlorpromazine already may have extrahepatic biliary obstruction. Needle biopsy of the liver in these and other cases in which the differential diagnosis is difficult may be of great value, but even after needle biopsy abdominal exploration may be necessary for the answer.

I have operated upon two patients who had jaundice produced by chlorpromazine. In both cases T-tube drainage of the common bile duct and cholecystostomy excluded extrahepatic obstruction and small gallstones, and in both cases the jaundice subsided in a progressive manner, probably owing to the fact that the dysfunction of the sphincter of Oddi contributed to the accumulation of bile-pigment debris within the extrahepatic biliary duct radicals and biliary stasis was relieved.

In other cases of jaundice in which the patient's symptoms and results of laboratory tests seemed to suggest an extrahepatic biliary obstruction, none was found and biopsy of the liver showed cholangiolitic inflammation, as described by Watson and Hoffbauer. This can occur also in cases of early biliary cirrhosis. Needle biopsy of the liver is helpful but, unfortunately, not completely diagnostic, for the same picture which it discloses may be seen in the presence of inflammatory lesions of the gallbladder, common bile duct, and pancreas secondary to certain obstructive lesions. In such instances, again, surgical exploration may be indicated.

In discussing these difficult problems of differential diagnosis with patients, I usually refer to the abdominal exploration as an additional test accompanied by little more risk than some laboratory tests, such as gastroscopy or even needle biopsy of the liver when obstructive jaundice is present. Fortunately, if drainage of the biliary tract is done at exploration by T-tube or cholecystostomy, the patient's condition more rapidly improves.

One must be careful, however, to be sure the patient does not have infectious hepatitis, for operation in the presence of infectious hepatitis is accompanied by a considerably increased operative risk, and the patient's condition is worsened, rather than bettered, by intervention.

Comment

It is impossible to include all the advances made in abdominal surgery in a paper of this length. My purpose has been to call to your attention some of the most important ones, particularly those which have involved the results of experimental studies in the laboratories correlated with clinical investigations in the hospitals, both of which processes, taken with the American plan of graduate training and standardization of accepted hospitals for such training, have placed American surgery in the ascendant position. Indeed, one might be so bold as to add, there is no reason that, with similar forethought and earnest application, the same happy objectives could not be attained in other scientific fields.

Section of Surgery.

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Massive Venous Thrombosis Associated with Incoagulability of the Blood

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This report emphasizes two aspects of the problem of venous thrombosis which have received very little documentation in the literature. Firstly, the development of marked thrombocytopenia and incoagulability of the blood in association with extensive thrombophlebitis is unusual. Secondly, the phenomenon of "heparin rebound," [1-4] which may have been of etiologic significance in the recrudescence and spread of venous thrombosis in this case, deserves reemphasis.

Report of a Case

A 79-year-old white man was admitted to St. Peter's General Hospital on Aug. 19, 1956. He was in apparent good health until three days before admission, when he fell, injuring his right leg. Later that day he developed swelling about that ankle, progressing gradually in the next few days to involve the calf and then the entire limb.

On physical examination, the right lower extremity was slightly cyanotic, considerably swollen from the inguinal crease downward, and warm to the touch. Pitting edema was noted over the dorsum of the foot and over the tibia. Homan's sign was equivocal. Arterial pulsations appeared normal.

Aside from a blood pressure of 160/90 and multiple subcutaneous lipomata over the extremities and trunk, there were no important findings. The admission diagnosis was right iliofemoral thrombophlebitis, precipitated by trauma.

The hemoglobin on admission was 79%, or 12.5 gm. per 100 cc. The hematocrit was 38%. The white blood cell count was 12,600, with 78% polymorphonuclear leukocytes, 14% nonsegmented. The urine showed 5 to 8 white cells per cubic millimeter and was otherwise negative. Blood urea nitrogen, sugar, and cholesterol were within normal limits. No admission platelet count or other blood studies were performed.

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From the Vascular and Medical Services of St. Peter's General Hospital.

Heparin therapy was instituted shortly after admission, intermittent injections of 50 to 75 mg. being given every six hours. Initially a clotting time of 40 minutes was achieved on this regimen, but not until the fourth hospital day was it steadily in the therapeutic range (Fig. 1).

By this time the right leg had become less swollen and less tender. By the sixth hospital day the limb appeared normal. The temperature, which had fluctuated between 99.4 and 102.2 F during the first four hospital days, had also returned to normal.

Ambulation, with snug elastic bandages, was begun. At this point the administration of heparin sodium was cut to 50 mg. every 12 hours and was continued in this intermittent fashion for an additional 2 days. No clotting-time determinations were made during this period.

Forty-eight hours from the time the heparin dosage was halved, on the eighth day of hospitalization, the right lower extremity was again noted to be increasingly swollen, painful, and approaching in appearance its admission status. Heparin therapy was reinstituted in increased dosage at intervals somewhat closer than every six hours (Fig. 1). On the 10th hospital day it was noted that blood failed to clot in any of the Lee-White test tubes even after observation periods extending over two hours. Heparin was abruptly discontinued for fear that the patient's tolerance to the anticoagulant might suddenly have decreased. That day the clotting time returned to 28 minutes, only again to become indefinitely prolonged. On the 11th hospital day, after the patient had had no heparin in 36 hours, his blood was still incoagulable. A platelet count was reported as 4000 per cubic millimeter. A second count, 18 hours later, was 2000 per cubic millimeter. Fresh blood transfusions were begun, and after one such transfusion a clotting time was 17 minutes with very poor clot formation. A second clotting time was in the same range (15 minutes), a very poor gelatinous, friable, incomplete clot again being observed.

Surgical consultation was sought at this time, and the consultant (N. R.) felt that the marked hypocoagulability of the blood indicated a possible depletion of circulating blood-coagulation factors, due to active and considerable thrombus formation in the leg and possibly elsewhere. The consultant

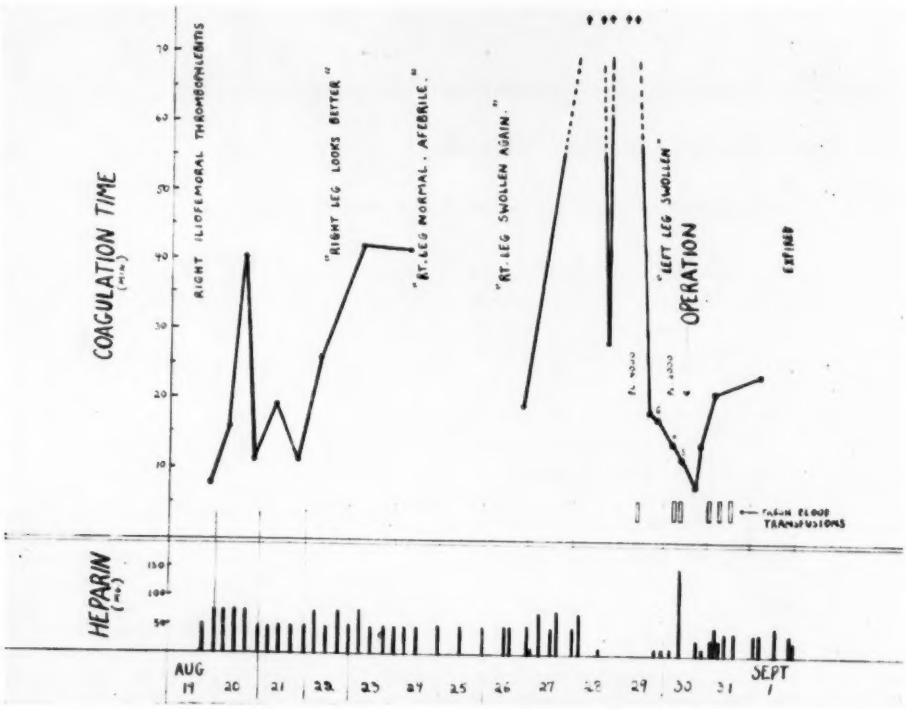

Fig. 1.—Clinical summary in graphic form, showing heparin dosage and Lee-White clotting times in relation to clinical course. *Pl*=platelet count per cubic millimeter; *G*, granular clot, and *S*, soft clot.

felt, too, that a strong possibility existed that a pulmonary embolus had occurred, in view of the recurrence of fever and the noticeable deterioration of the patient's general condition. It was suggested that if the coagulation time could be brought into a normal range by fresh blood transfusions, ligation of the inferior vena cava should be considered to arrest the ascent of the thrombotic process and prevent future embolization to the lungs. After the patient had received a total of 3 units of fresh blood, the Lee-White time was reported as 11 minutes, with soft-clot formation. Operation was decided upon and proceeded with on the afternoon of the 12th hospital day.

Operation.—Under tetracaine (Pontocaine) and dextrose spinal anesthesia, the inferior vena cava was approached through a right-oblique-muscle-splitting extraperitoneal incision. Moderate oozing was encountered in the retroperitoneal space, no definite bleeding points being observed. This ooze seemed to be adequately controlled by light pressure with moist gauze pads. The inferior vena cava was mobilized above the iliac bifurcation and a piece of umbilical tape placed about it. The vein was found to be thrombosed throughout its entire extent in the operative field, the iliac veins being also involved. The thrombus appeared firm with considerable acute and subacute surrounding perivenous inflammatory reaction. It was considered that thrombectomy would be too hazardous a procedure, and probably unproductive in view of the wide extent of the thrombotic and perivenous inflammatory process, both proximally and distally beyond the limits of the operating field. The wound was therefore closed without drainage. The retroperitoneal ooze seemed to have been controlled, and the field was dry at the end of the operation. Five hundred cubic centimeters of fresh blood was slowly administered during the course of this 75-minute procedure.

Because the operative findings seemed to substantiate the surgeon's preoperative impression, heparin sodium was cautiously begun again shortly after surgery with the administration of very small doses, no greater than 50 mg., and mostly given by dilute intravenous infusion. The Lee-White clotting times from the time of surgery to death, two days later, ranged from 7 to 22 minutes.

After operation, the patient gradually developed hypotension. There was an associated steady in-

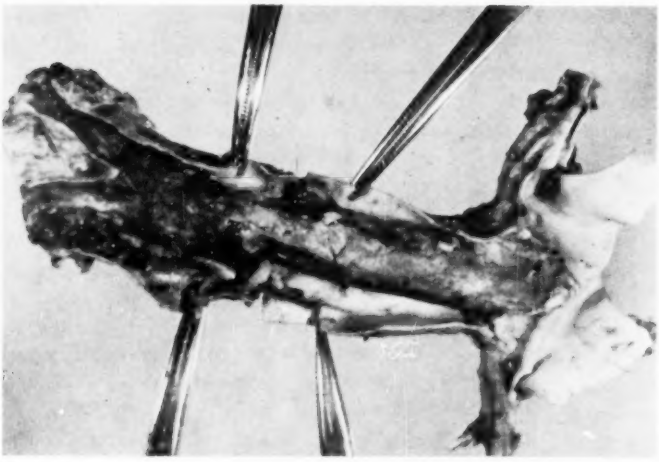

Fig. 2.—Gross appearance of thrombus in inferior vena cava and iliac veins. Note extension upward to level of renal veins. Formalin fixation.

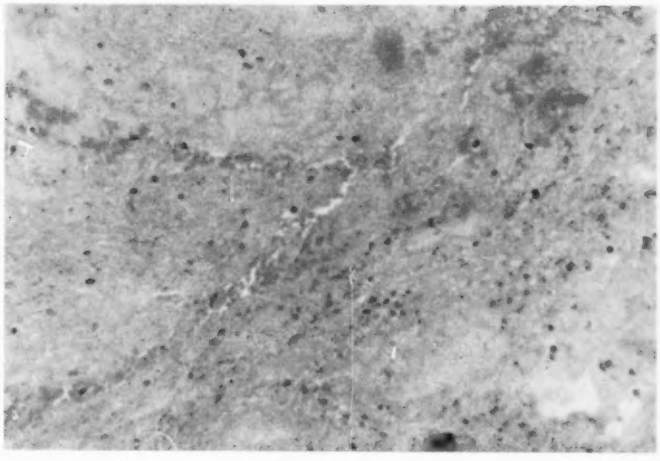

Fig. 3. — Photomicrograph of thrombus, showing predominant platelet composition.

crease in the swelling of the lower extremities, and it was felt initially that plasma loss into the limbs was responsible for the lowering of blood pressure. Three pints (1500 cc.) of fresh blood was administered during the first postoperative day and appeared to control the hypotension. The clotting times remained only slightly above normal. By the second postoperative day, however, his condition again deteriorated with a progressive fall in blood pressure, unrelieved by vasopressor drugs or other supportive treatment; and the patient died in shock.

Portmortem Examination.—The immediate cause of death was apparently a large retroperitoneal hemorrhage, approximating 2000 cc. in volume. This blood had failed to clot. The inferior vena cava and the iliac veins were completely occluded by firm, adherent thrombus, the upper end of which seemed to be floating freely in the lumen at the level of the renal veins, with a loose attachment to the main thrombotic mass (Fig. 2). A pulmonary embolus occluded the lower-lobe branch of the right pulmonary artery. No pulmonary infarction was present. Microscopic examination of the thrombus and the pulmonary embolus revealed them to be composed mainly of agglutinated platelets (Fig. 3).

The frequency of administration of heparin to this patient seems to have been low initially. In intermittent therapy a four-hour schedule is generally to be preferred. However, an adequate elevation of the coagulation time had been eventually achieved, with an associated drop in temperature and fairly rapid improvement in the appearance of the limb. While the frequency of heparin administration was

halved and the agent not discontinued suddenly, the decrease in frequency of injections to a twice-daily schedule probably represented a fairly sudden diminution in the concentration of circulating anticoagulant.

General Comment

Thrombocytopenia in association with widespread thrombosis of small blood vessels has been reported. Indeed, the syndrome of "thrombotic thrombocytopenia" with platelet thrombosis has been well documented since its first description by Moschcowitz in 1925.[5,6] However, in this condition the thrombi are mainly distributed in arterioles, capillaries, and venules.

Allen[7] stated that thrombocytopenia (60,000-70,000 per cubic millimeter) may occur in extensive thrombotic disease, particularly when the major arteries collect large platelet thrombi on arteriosclerotic plaques. Blaustein and Wright[8] observed thrombocytopenia in a patient with phlebitis. However, we have been unable to find a case in which the thrombocytopenia had been so marked and the associated coagulation defect so severe as to produce a state of practical incoagulability of the blood, as measured by routine laboratory tests.

It seems logical to assume that in the formation of the massive amount of thrombus other coagulation factors (fibrinogen, prothrombin, etc.) may well have been withdrawn from the circulation with the platelets.

Of possible etiologic significance in the massive thrombotic relapse is the so-called "heparin rebound" phenomenon, the long-postulated period of hypercoagulability of the blood which is said to follow the abrupt cessation of heparin therapy, or perhaps even the abrupt diminution in dosage, as this case seems to illustrate. Certainly the recrudescence of symptoms and signs in this case followed a cut in dosage frequency by approximately 48 hours, this latent period being in agreement with the experimental observations of Cate et al.[4] and with the clinical observations of Crafoord and Jorpes, de Takats, and Artz and Pulaski.[1-3]

Cate has listed the various etiologic factors involved in recurrent thrombophlebitis or embolism after apparently effective therapy as (1) clinically undetectable residual disease secondary to inadequate heparinization either in dosage or in longevity of treatment, (2) continued venous stasis associated with a nonambulatory patient, and (3) a postulated period of hypercoagulability of the blood of a rebound nature following the abrupt cessation of heparin ("heparin rebound").

This case report therefore serves once again to emphasize the following basic tenets of active heparin therapy of thrombotic states:

(*a*) Treatment with heparin, once begun, must be in adequate dosage (to keep the coagulation time in the "two to three times normal" range), and, if intermittent therapy is employed, should be at short enough (i. e., four-hour) intervals.

(*b*) Treatment should be continued until such time as the therapeutic response shall have been achieved, and until the patient shall have, in addition, been actively ambulatory for at least a week.

(*c*) Therapy should be discontinued gradually.

Summary and Conclusions

A case of massive venous thrombosis in the lower extremities and inferior vena cava is presented, associated with incoagulability of the blood and marked thrombocytopenia.

Exhaustion of circulating blood-coagulation factors by the extensive thrombotic process is postulated.

The possible triggering role of the "heparin rebound" phenomenon is discussed.

10 Lincoln Ave., Highland Park, N. J. (Dr. Rosenberg).

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Correction

In the article "Use of Enzyme-Digested Heterografts as Segmental Arterial Substitutes: III. Follow-Up Observations on Two-Year-Old Aortic Implants," by Dr. Norman Rosenberg and colleagues, in the February, 1958, issue of THE ARCHIVES (p. 275), mislabeling of the cuts comprising Figure 3 caused incorrect insertions; the printed legends are correct for each part of the Figure. The cuts for parts A and D should be interchanged; also the cuts for parts C and D.

A Maneuver of Help in Diagnosis of Ruptured Disk

BERNARD C. SHERBOK, M.D., Denver

Any test which may yield additional evidence in differentiating the syndrome of ruptured intervertebral disk from low back conditions with similar clinical pictures should be a welcome addition to one's armamentarium. At present several tests are in use, the most frequently practiced being the straight-leg raising, Lasègue, jugular compression, and sciatic-nerve-stretching tests. Aird and Naffziger [1] and Aird [2] suggested a test which may also be employed. They modified the standard digital jugular compression test by placing a blood pressure cuff around the neck and inflating it to 40 mm. Hg. They recommended keeping the cuff inflated for 10 minutes, since in some cases positive results did not occur for as long as seven or eight minutes. Bradford and Spurling,[3] however, disagree with this time interval and claim that important observations are not made after the first 30 seconds. The significant point in this test is that not only the back pain but also the radicular pain must be evoked.

Since 1944 I have been using a simple procedure in attempting to differentiate low back pain with radiation into the lower extremity caused by rupture of the intervertebral disk from conditions which may simulate it. This procedure has been a valuable aid and is much simpler to perform than the Aird-Naffziger test.

Technique

The test may be performed in the supine, sitting, or standing position. The nature of the test and its interpretation should be explained to the patient before starting in order that he may know what to expect. The patient is asked to take a deep breath through the mouth. He should then hold his nostrils tightly closed between the thumb and index finger and, with the lips closed, should attempt to exhale through the nose until a sensation of popping of the ear drum membranes is experienced. Attempted exhalation should be continued for several seconds. During this period the test is considered to be positive only if the low back pain and radicular radiation are evoked or aggravated. Occasionally the pain is not produced until the instant of release of compression. This procedure should be repeated in the various positions mentioned before the result is evaluated.

Comment

It is a well-known fact that coughing, sneezing, or straining at stool frequently exaggerates low-back and radicular pain (Dandy [4]). This question is asked routinely in obtaining the history in any problem of low back ache, especially in those cases in which referred pain is present. The mechanism of pain production in these acts, as well as the jugular compression and the Aird-Naffziger test, is the same. The blood in the jugular veins is held back for varying intervals of time, ranging from momentarily, in the case of sneezing, to 10 minutes in the Aird-Naffziger test. The increase in pressure within the jugular veins is then reflected immediately within the cranial chamber, where a rise in the pressure is produced. This rise in pressure is, in turn, reflected at once in the lumbar cerebrospinal fluid, since, normally, there is free communication between the cerebral and the spinal subarachnoid spaces. The resulting

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increase in pressure aggravates the mechanical stress on a nerve root which is compressed by a herniation of the nucleus pulposus. When the test is performed either in the sitting or in the standing position, the additional factor of the force of gravity of the spinal fluid may evoke a positive response in some instances in which the test is negative in the supine position.

The increase in intracranial pressure, and therefore in the intraspinal pressure in the test described, is produced by forced exhalation, which causes increased intrathoracic pressure. This test is a performance of the Valsalva maneuver.

It must be emphasized that this test is only one of many which an examiner should perform in attempting to arrive at a diagnosis of herniation of the nucleus pulposus. The interpretation of the test must be made in the light of the history and physical findings as a whole. A negative result in cases in which there is a suggestive history coupled with significant physical findings should not preclude an exploratory laminectomy. A positive result, however, becomes especially important whenever it dovetails with other confirmatory evidence.

Summary

A simple technique for increasing the intraspinal pressure in suspected cases of ruptured disk is described. This test has proved useful as an aid in corroborating the presence or absence of this condition when properly evaluated along with other data in the examination of the patient.

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Intrahepatic Cholangiojejunostomy for Biliary Obstruction

Long-Term Follow-Up Study of a Case

HARRIS B. SHUMACKER Jr., M.D., and JACK MILLER, M.D., Indianapolis

In 1948 Longmire and Sanford [1] proposed a method of treating biliary obstruction by intrahepatic cholangiojejunostomy following partial resection of the left lobe of the liver. In 1956 Longmire and Lippman [2] reviewed their own experiences and those of others reported in the literature. This survey included a total of 28 patients, 19 of whom were treated for benign biliary obstruction and 9 for malignant obstruction. Since the development of this procedure, nearly 10 years ago, few long-term follow-up studies have been recorded in the literature. Most of the patients so treated had been followed for only a few months after operation at the time of the report. The longest follow-up was for a period of 5 years 11 months. This patient ultimately died of recurrent episodes of cholangitis. The present report concerns a patient treated for benign postoperative biliary obstruction approximately six and a half years ago. This case was mentioned in the report of Longmire and Lippman.

Submitted for publication Jan. 6, 1958.

From the Department of Surgery, Indiana University Medical Center.

Report of Case

The patient, a 30-year-old woman, was first seen on May 1, 1950, complaining of chills, fever, and jaundice. In 1945 a cholecystectomy had been performed in another institution. Jaundice appeared on the third postoperative day and never completely cleared thereafter. She suffered intermittent episodes of cholangitis. In 1947 an exploratory laparotomy was carried out in another institution. The common hepatic duct was found to be markedly dilated. Distally there was complete obliteration of the duct over a distance of about 0.5 cm. and below this a collapsed, but patent, common duct. The continuity of the hepatic and common ducts was reestablished by plastic repair. The liver at this time was noted to be greatly enlarged. She did well until the T-tube was removed, three months later, and then she began to have recurrent bouts of cholangitis. By 1949, in addition to jaundice, she noted ascites, ankle edema, and pallor. A few weeks prior to admission, in May, 1950, she had passed a large, tarry stool, and on one occasion sometime after admission she vomited blood.

Physical examination revealed the patient to be chronically ill and deeply icteric. The essential positive findings included marked enlargement of the liver, which was firm and extended 8 or 9 cm. below the right costal margin; marked splenomegaly, and prominent ascites. The hemoglobin was 6 gm. per 100 cc.; the erythrocyte count, 2,200,000, and the leukocyte count, 1500, with a

Liver Function Studies

Time	1950		1951		1952	1953 *	1954–1956	1957
	Before Splenectomy	After Splenectomy	Before Operation	After Operation				
Serum bilirubin, mg/100 cc.	6.3→15.5	8.2→4.1	11.5	7.6→2.9	2.1	8.4	1.3→0.6	1.1
Alkaline phosphatase, units	26	26	82		36.0	28.6	35	21.6
Prothrombin, % of normal	42	100	100	100	100	100	100	100
Cephalin flocculation	2+	2+	1+	2+	2+	2+	2+	3+
Thymol turbidity, units	6	5.5	5.5	--	7	4	--	3.5
Total serum proteins, gm/100 cc.	5.6	4.1	4.1	7.0	6.9	6.0	7.4	6.5
Serum albumin, gm/100 cc.	3.9	2.7	2.7	3.7	4.0	3.4	4.0	4.2
Sulfobromophthalein, %	--	--	31		26		24	42→24

* During episode of cholangitis.

normal differential. The platelet count was 61,000 per cubic millimeter, and the bone marrow was generally hyperplastic. Liver function studies were abnormal (Table). Urine urobilinogen was reported as 4.3 mg. per 100 cc., and a few days later a quantitative urine urobilinogen determination was negative. The stool examination was positive for occult blood, positive for bilirubin and urobilinogen, and negative for urobilin. A few days later a stool specimen was reported to have no urobilinogen. X-ray studies, including chest film, barium enema, and upper gastrointestinal series, were normal except for the enlarged liver and spleen and questionable evidence of esophageal varicosities.

It was concluded that the patient had biliary obstruction with biliary cirrhosis, marked hypersplenism, and questionable portal hypertension and esophageal varicosities.

On June 5, through a left thoracoabdominal incision, a splenectomy and splenorenal anastomosis were performed. Portal pressure was measured at 320 mm. of water at this time. A liver biopsy revealed advanced biliary cirrhosis. The spleen weighed 1520 gm. The response to splenectomy was gratifying (Fig. 1). She was discharged from the hospital on a regimen including vitamin K and iron therapy.

Approximately 11 months later, on May 22, 1951, she was readmitted for treatment of diarrhea. Once again she had normochromic anemia and severe derangement of liver function. X-rays on this occasion revealed no evidence of esophageal varicosities. After discharge from the hospital she developed a severe bout of cholangitis and her condition in general deteriorated appreciably.

She was transferred from another hospital on Aug. 15, 1951. She was emaciated and looked critically ill. Her liver edge was palpable approximately 10 cm. below the right costal margin. There was obvious ascites. She gave a recent history of generalized crampy abdominal pain and obstipation. X-ray studies and physical examination pointed to a complete obstruction in the region of the splenic flexure. Shortly after admission a cecostomy was performed. At this time 5 liters of ascitic fluid was removed. She had adequate decompression with the cecostomy and shortly thereafter began to have bowel movements again. In considering surgical correction of her chronic biliary obstruction, it seemed unlikely that she could withstand a long and difficult surgical procedure. She had profound weakness. In spite of the presence of ascites and edema, her weight had dropped to approximately 80 lb. It was feared that efforts to dissect out and reconstruct a pathway from the common hepatic duct into the gastrointestinal tract might prove very difficult, and it was finally decided that she might better withstand, and might have an appreciably better chance of a good result from, an intrahepatic cholangiojejunostomy.

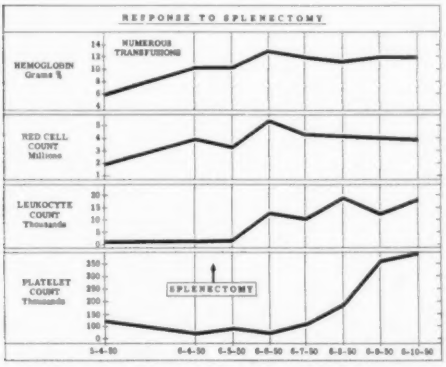

Fig. 1.—Chart showing response to splenectomy.

This was carried out on Aug. 31. The liver was found to be huge in size and markedly cirrhotic. No tumor mass or obstruction of the colon was demonstrated. The stomach and duodenum were densely adherent to the undersurface of the right lobe of the liver. Initial efforts at carrying the dissection down toward the region of the common duct convinced us that this attack would be unusually difficult and that intrahepatic cholangiojejunostomy would be a great deal easier. A very generous portion of the left lobe of the liver was resected. Once a fairly large intrahepatic bile duct was encountered, cholangiography was performed. This revealed considerable dilatation of the ductal system both on the right and on the left side with free communication between the right and the left main hepatic duct and a complete block of the common hepatic duct just beyond the point of union of the two branch ducts. A Roux-Y limb of jejunum was constructed, about 15 in. in length. The incision in the jejunum was then sutured to the bile duct with fine interrupted nonabsorbable surgical (silk) sutures. The anastomosis was somewhat difficult because of the thin wall of the bile duct and the dense scarring of the surrounding liver. A fair mucosa-to-mucosa approximation was accomplished. A rubber catheter was left through the anastomosis. It extended a short way into the bile duct and a longer distance down into the jejunum. The jejunum was then carefully sutured to the margins of the cut edge of the liver. Her postoperative convalescence was stormy, but she made progress from day to day. Because of a left pleural effusion, several thoracenteses were necessary. A wound abscess required incision and drainage three weeks after operation. She was finally discharged from the hospital, on the 34th postoperative day. By this time her serum bilirubin

had fallen to 3.6 mg. per 100 cc., and her weight had risen to 99 lb.

She continued to improve. Two weeks following discharge she passed an object at stool which she thought was the catheter that had been left through the anastomosis. Her markedly improved status was evident not only in her sense of well-being but also in her weight gain and hepatic function studies (Table; Fig. 2). She was readmitted June 30, 1952. At this time she was four months' pregnant. She ultimately had a premature, spontaneous delivery at six months. The child was not viable. At the time of the June admission her liver had regressed in size so that its edge was palpable about 5 cm. below the right costal margin.

She was next admitted on Nov. 4, 1953, with a six weeks' history of chills, fever, and recurrence of jaundice. Her liver was somewhat larger than it had been on the last admission. X-ray of the abdomen revealed that the catheter which had been thought to have passed long before was still in place. It was felt that the catheter might well be obstructed and responsible for the episode of cholangitis. On Jan. 14, 1954, a laparotomy was again performed. The catheter was removed through a small incision in the jejunum. It was completely obstructed with "biliary mud." After its removal and a thorough irrigation, there was a copious flow of bile. A cholangiogram was made (Fig. 3). This revealed opacification of the entire

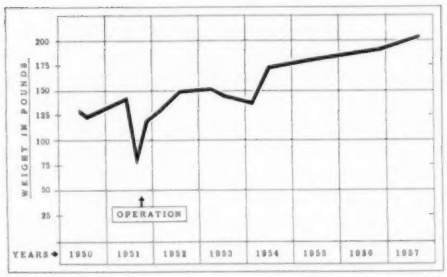

Fig. 2.—Chart showing weight gain following surgical treatment.

intrahepatic biliary tree and the same obstruction of the common hepatic duct as that noted on the previous cholangiogram. There was no significant diminution in the size of the main hepatic ducts or of their branches as compared with that shown in the cholangiogram obtained at the time of cholangiojejunostomy. Liver biopsy again revealed evidence of marked biliary cirrhosis.

Two months later she was admitted to another hospital with a brief episode of what was considered possibly cholangitis. She has had no subsequent episodes of this sort. She has been hospitalized, however, on two occasions since then. In July, 1955, she was admitted to the hospital because of the presence of a ventral hernia, complicated by a walled-off abscess within the hernial

Fig. 3.—Cholangiogram made 26 months after intrahepatic cholangiojejunostomy.

sac. The herniated omentum walling off the abscess cavity was excised and the hernia repaired. In May, 1956, she was again hospitalized, for delivery of a viable female infant.

The patient has been followed closely during the past four years and has remained remarkably well. There has been no clinical evidence of icterus. The liver is barely palpable 1 or 2 cm. below the right costal margin. She has no evidence of anemia. Her principal difficulty is with obesity. She has gained from a low of 80 lb. to a present weight of 204 lb. (Fig. 3). In spite of the excellent clinical course and the marked reduction in liver size, hepatic function studies are still abnormal.

Comment

Benign common-duct obstruction often presents a difficult therapeutic problem. We are in agreement with others that the primary effort should be to reconstruct the continuity of the common duct and, if this is impossible, attempt to provide a new shunt between the dilated proximal segment and the intestinal tract, preferably through a Roux-Y jejunostomy. When such procedures fail, the intrahepatic cholangiojejunostomy of Longmire and Sanford provides the surgeon with an alternative method which may restore good health to the patient. This may be the procedure of choice in cases in which efforts at direct reestablishment of biliary-gastrointestinal continuity have repeatedly been futile, or in cases in which such an effort has given the operator the impression that an adequate repair of this sort is technically impossible. In the case reported, the procedure was carried out by election, in spite of the fact that only one previous effort had been made to reestablish common-duct continuity because it seemed that the critically ill, emaciated patient could better withstand this procedure and that it would offer a more favorable outlook for adequate biliary drainage. This case has been recorded in some detail because of the paucity of long-term follow-up observations after such treatment. The operation has proved eminently satisfactory in this case for a period of over six and one-half years. The only episode of cholangitis which has occurred since operation was apparently associated with plugging of the catheter left in place through the line of anastomosis. A second possible episode took place a few weeks after removal of the catheter. It is our feeling that it is wise to leave a catheter through the site of anastomosis, but that one should bring the distal end of the catheter out through the jejunal limb and the abdominal wall, so that it can be easily removed at a subsequent date. The desperately ill patient here reported has gained approximately 120 lb. since operation and has had two pregnancies. Following operation there was a prompt fall in serum bilirubin. It has remained within normal limits except for the period during which she had cholangitis, a year after operation. Prothrombin time has returned to normal, as have the total serum protein and the albumin-globulin ratio. In spite of the absence of jaundice and the marked diminution in the size of the liver, some evidences of hepatic dysfunction persist.

Summary

A case of complete biliary obstruction secondary to cholecystectomy which was successfully treated by intrahepatic cholangiojejunostomy is reported. During a follow-up of six and one-half years the patient has enjoyed good health. In spite of the marked diminution in the size of the liver and the absence of jaundice, hepatic function studies remain abnormal.

Dr. R. P. Bissonnette, of Evansville, Ind., referred the patient for treatment and has helped very much in following her carefully during the years since her surgery.

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Amputations of the Lower Extremity for Arteriosclerosis

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This paper is a review of the amputations of the lower extremity done at the Louisville Veterans' Administration Hospital from its opening, in April, 1946, to July, 1956, for arteriosclerosis with and without diabetes. Amputations for other disease processes are excluded.

Those patients who comprised this study were all men and were mostly in the older age groups with arteriosclerosis and adult diabetes. The last feature exists because juvenile diabetics would have been rejected from military service had they been diagnosed as diabetics at the time of their induction.

The study includes a series of 89 patients with major and minor amputations resulting from vascular insufficiency secondary to arteriosclerosis. Recently, with the advent of arterial reconstruction, each patient has been evaluated for possible arterial grafting to increase the blood supply to the affected extremity.

Forty-seven sympathectomies were done prior to amputation, without mortality and with minimum morbidity. Eight patients had bilateral sympathectomy because of symptoms in the opposite leg.

The results of these sympathectomies are difficult to evaluate, but observers, such as Edwards, of Boston,[1] and Shumacker, of Indianapolis,[2] believe that lumbar sympathectomy is of real value in the prevention of gangrene and in healing of superficial necrosis and ulceration. It is also a useful procedure in certain cases, helping to make a lower amputation successful. Pratt,[3] after a study of 309 cases, found that if symptoms are those of claudication and coldness, 95% will avoid amputation if sympathectomy is done. If gangrene is present, 66% will have an amputation.

We feel that sympathectomy has permitted us to amputate successfully at a lower level, with primary healing, in some cases, and in other cases to avoid amputation altogether. Since our total number of sympathectomies has not formed a part of this study, these impressions are clinical only. We have, like many others, tried various chemical vasodilators, such as intra-arterial histamine, intravenous ether, and tolazoline (Priscoline), without appreciable benefit.

Surgical Procedure

Our indications for amputation have been any or all of the following: gangrene, uncontrolled pain at rest, or uncontrolled infection. Toes were amputated using a fish-mouth type of incision, which was usually left open. In the transmetatarsal amputations the McKittrick technique, with a long plantar flap, was used. Below-the-knee amputations were done in the prone position without a tourniquet, using the method described by Silbert,[4] except that the long amputation knife was used instead of the scalpel where possible.

In the above-the-knee amputation, we have adopted several principles. Equal, short anterior and posterior flaps (two-thirds of the radius of the thigh at that level) are marked out to conserve maximum blood supply. The scalpel is used only to carry the incision into the subcutaneous tissue

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but not through the fascia. The long amputation knife is used to divide the remaining soft tissue with a clean sweep, which we feel preferable to the unavoidable handling and chopping of scalpel dissection. The muscle flap should be ⅛ to ¼ in. shorter than the skin flap. The bone is sawed at the same level as the apex between the skin flaps; or if it is apparent that this will result in tension of closure, it should be shortened approximately ½ in. The periosteum should be circumcised at the saw level, but not otherwise stripped away. The main vessels are ligated just above the cut section of muscle with a light nonabsorbable suture. Nerves should be gently pulled down and divided with a sharp knife, and only individual nutrient vessels should be ligated. The wound is now thoroughly irrigated with sterile saline. Handling has been kept to a minimum. In closing the wound, the fascia is approximated loosely with interrupted fine-as-possible, nonabsorbable sutures without drainage. Interrupted fine steel wire is used in the skin. Skin traction is employed only if a borderline degree of tension of flaps persists.

Ninety-five per cent of the amputations were done under spinal anesthesia. No tourniquets are necessary in this type of patient, and only minimal finger pressure is necessary over the femoral artery in a few cases.

Results and Comment

The age distribution in diabetics and nondiabetics is shown in Table 1. Diabetic patients had 35 amputations and nondiabetic patients 54 amputations. Ages ranged from a younger to an older age in the nondiabetic than in the diabetic group, but there was little essential difference in their mean ages, with the majority of both groups in the 50- to 70-year age bracket. This is in agreement with the findings of Shumacker[2] and Kendrick.[5] However, it is generally believed that the diabetic amputee is approximately 10 years younger than the nondiabetic amputee.

TABLE 1.—*Age Distribution of the Patients*

	Diabetic		Nondiabetic	
Age	No.	Per Cent	No.	Per Cent
30-40	0	0	1	1.9
40-50	0	0	3	5.5
50-60	17	48.5	24	44.0
60-70	16	45.7	20	37.0
70-80	2	5.7	5	9.2
80-90	0	0	1	1.9
Total	35	Total	54	

TABLE 2.—*Total Amputations in Eighty-Nine Patients*

	Number	Successful	Unsuccessful
Great toes Other toes	13 16	11	18
Transmetatarsals	7	2	5
Syme amputations	1	1	0
Below-knee amputation	47	41	6
Above-knee amputation	71	70	1
Total	155	125	30

In evaluating the surgical results, it should be pointed out that there were many adverse factors present in this series of patients. Forty-three had preexisting cardiac disease; a number were in frank failure; fourteen had had previous cerebral vascular accidents. In numerous instances the patients came from a low economic level and entered in a poor state of nutrition. Many exhibited combinations of advanced degenerative diseases.

In this series of 89 patients there was a total of 155 amputations. There were 29 toe amputations, of which 11 were successful; 18 patients required a higher level of amputation. Only one of the successful amputations and six of the failures had been preceded by a sympathectomy.

We feel that a minor amputation should be tried if there is a chance of success, since 39% such amputations were successful and these patients were definitely better off because they were able to ambulate without the aid of an artificial appliance. Our indication for toe amputation is gangrene limited to the distal part of one toe without osteomyelitis, infection or edema of the foot, and absence of rest pain.

Of the seven transmetatarsal amputations, two only were successful, and the single Syme amputation was successful. Very few patients were candidates for these low amputations because of the extensive degree of gangrene or infection, or because of uncontrolled rest pain.

Below-the-knee amputations totaled 47, of which 41 were successful, but 2 required a minor revision. Four required a higher amputation.

It is felt by Kendrick [5] and others that a below-the-knee prosthesis is more satisfactory than an above-the-knee prosthesis. Even without prostheses, below-the-knee amputees have better balance in their wheel chairs. With respect to this, of the 47 patients with below-the-knee amputations, 23 were fitted with a satisfactory appliance, and 2 of these are ambulatory with bilateral prostheses. Fourteen required wheel chairs.

Most of the 14 patients not fitted with artificial limbs were prevented from this type of ambulation by their physical condition, such as previous cerebral vascular accidents and cardiac disease. One or two refused prostheses.

We have tried to evaluate our patients preoperatively as to feasibility of a closed below-the-knee amputation. However, we have been unable to do so. By experience we have found the following clear contraindications to a below-the-knee amputation: (1) infection near the proposed incision; (2) abrupt temperature change above the proposed incision; (3) flexion contracture of the knee; (4) absence of femoral pulse, and (5) scanty bleeding at time of surgery, especially of the subcutaneous tissues. At surgery, if good vascularity is observed, healing is assured. But occasionally, with greatly diminished blood supply, primary healing has been observed.

Of the 35 below-the-knee amputations that healed primarily, 21 had had a previous sympathectomy; 14 had not had a sympathectomy. Six had delayed healing; two required revision, and four required reamputation above the knee. Only two of these with complications had not had a sympathectomy. Nine patients later required a major amputation on the opposite leg.

Of 71 patients with above-the-knee amputations, 5 died in the postoperative period, and these constitute our entire mortality. Fifty-six healed primarily; nine had delayed healing, and only one required a higher amputation.

Of these 66 surviving patients, 21 were fitted with an above-the-knee prosthesis, and 27 were given wheel chairs. Ten patients have had a bilateral above-the-knee amputation, and one of these ran a barber shop for several years, wearing his bilateral prosthesis. As in the case of the below-the-knee amputees, many of these patients were prevented by physical disability from wearing prostheses.

As is easily seen here, the higher the amputation level the greater the chances of obtaining primary wound healing. However, we still try to preserve as much useful limb as possible and feel that the results justify this.

Ten patients have had bilateral above-the-knee amputations, and eight patients have had bilateral below-the-knee amputations. Two patients had an above-the-knee amputation on one side with a below-the-knee amputation on the other. This illustrates the severe generalized nature of the occlusive vascular disease in this group.

There were 5 * postoperative deaths, a mortality of 6.1% among 82 patients with major amputations. If the mortality were based upon the 118 major amputations, it would be 4.2%. These five patients were in

* Eight died with healed wounds during the period of hospitalization of unrelated diseases.

TABLE 3.—*Postoperative Deaths*

Patient	Age	Disease	Extremity Amputated *	Cause of Death	Days Postop.
1	62	Arteriosclerosis	A-K left	Cardiac arrest at surgery	3
2	69	Arteriosclerosis	A-K left	Coronary occlusion	15
3	57	Diabetes	A-K left	Uremia	9
4	55	Arteriosclerosis	A-K right	TB	21
5	74	Arteriosclerosis	A-K right	Pulmonary embolism	1

* A-K means above-the-knee amputation.

TABLE 4.—*Long-Term Follow-Up of Eighty-Four Patients Surviving Amputation*

Follow-Up, Mo.	No. Followed	Deaths	Per Cent
0-12	84	13	15.5
12-24	71	5	7.0
24-36	66	3	4.5
36-48	63	1	1.5
48-60	60	2	3.3
60-100	58	1	1.8
Unknown	..	2	2.3
Total	84	27	32.1%

a precarious condition prior to surgery, and all had extensive gangrene, necessitating an above-the-knee amputation. This mortality is the lowest we have noted except for that of Shumacker,[2] who reports a mortality of 2.7%. Most authors report a mortality of 10% or higher.

Thirteen patients, or 15.5% of the 84 postoperative amputees, died during the first year after surgery.† Five more died the second year, raising the mortality to 22.5% for the first two postoperative years. Thereafter, the mortality rate declines rather sharply, the total deaths thus far in a follow-up period of 11 months to 10 years being 27, or 32.1% of the entire group. This would probably be higher if we had a complete follow-up. We believe this high initial death rate points to an early demise of those with severe cerebral and coronary sclerosis, leaving a residual group with reasonable cardiac reserve rendered comparatively inactive by their amputation.

Conclusions

It will be recalled that 41 of the 47 below-the-knee amputations and 70 of the 71 thigh amputations were successful and that primary healing occurred in 74% of the former and in 79% of the latter. This relatively good wound behavior we attribute in large measure to the use of the long amputation knife, allowing minimal tissue trauma and handling.

Good wound healing would partly explain the low operative mortality of 6.1%. Other contributing factors we believe lie in good nursing care and in the attention to the details of wound dressings, nutrition, and fluid and electrolyte balance in these elderly, debilitated patients.

Our conservatism in amputation cost a number of patients extra amputations and prolonged hospitalization; but, as it happened, none of the postoperative deaths followed reamputations. On the positive side of the ledger, the 39% successful digital amputations and 87% successful below-the-knee amputations speak for themselves. We only wish there were surer methods of predicting before operation when an amputation wound at a given site will heal.

The results in the present group of patients, of whom nearly one-quarter died in the first two postoperative years, corroborate the findings of others as to the poor life expectancy of patients coming to major amputation for vascular insufficiency.

We can thus far offer only a clinical appraisal of the value of sympathectomy in these patients. In a number of cases it put off amputation two years or longer. In others it seemed to promote better wound healing or to allow a lower site of amputation. Our policy at present, especially as there have been no deaths or serious complications following sympathectomy, is to employ it whenever there is reasonable likelihood that it will be of benefit.

Summary

From April, 1946, to July, 1956, a total of 89 patients in this hospital have undergone 155 major and minor amputations of the lower extremity for senile and diabetic arteriosclerosis.

These amputations comprise 71 above-the-knee, 47 below-the-knee, 1 Syme, 7 transmetatarsal, and 29 toe amputations.

There was no significant age difference between the diabetic and the nondiabetic patients.

There have been 5 postoperative deaths, all occurring among the 71 above-the-knee amputations. There was a patient mortality of 6.1% and an operation mortality of 4.2% for the 118 major amputations.

Of the 71 above-the-knee amputations, 70 were successful, and 41 of the 47 below-the-knee amputations were successful.

Sympathectomy has been used frequently before amputation. No deaths or serious complications have occurred, but final evaluation must await further analysis.

† Six patients have been lost in follow-up. Seventy-eight, or 93%, have been followed from one to eight years.

The details of the operative technique are presented.

Veterans' Administration Hospital.

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Tissue Reaction to Plastics

A Comparison of Nylon, Orlon, Dacron, Teflon, and Marlex

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Marlex 50 polyethylene is a new plastic recently developed by Phillips Petroleum Company, Bartlesville, Okla. It is significantly different in a number of important respects from the familiar "squeeze-bottle" polyethylene. The new plastic is produced from ethylene gas in a carrier solution by catalytic action at relatively low pressures. After separation from catalyst and solvent, the resulting solid product has the same appearance as conventional polyethylene. However, the new plastic has a highly crystalline molecular structure, affording an unusually high softening temperature and high tensile strength as compared with conventional material. By hot-melt extrusion at 400 to 600 F through an orifice, Marlex 50 polyethylene is readily made into monofilament. Cloth made from this fiber is impervious to water and possesses outstanding chemical resistance. It has a softening temperature of 260 F, allowing it to be sterilized in an autoclave with no damage. The tensile strength of Marlex monofilament is exceptional—50,000 to 150,000 lb. per square inch—the exact value being a function of cooling rate and drawing conditions during manufacture. These values may be compared with 65,000 to 114,000 lb. for nylon, 47,000 lb. for Teflon, 81,000-124,000 lb. for Dacron, and 45,000-83,000 lb. for silk.[1,4,5]

In order to compare the tissue reaction of Marlex with that of some of the other plastics in current use, the method used by the U. S. Bureau of Mines[3] to test the foreign-body reaction of industrial dusts was employed. LeVeen[2] used this technique in comparing the tissue reaction of Teflon with that of other plastics and considered it a more sensitive test than subcutaneous implantation. In this test, the plastic (in the form of small particles or pellets) was implanted intraperitoneally in dogs, and seven days later the animals were killed and the intra-abdominal viscera examined grossly for adhesions and other evidence of inflammary reaction. Microscopic studies were also made of the tissues for confirmation of the gross findings.

Material and Method

Fifteen dogs were used in this experiment. Marlex was used in the form of tiny pellets, and the other plastics (nylon, Orlon, Dacron, and Teflon) were used in the form of the undyed shredded yarn, pellets or small particles not being available. The plastics were boiled with a detergent and rinsed with distilled water to remove surface contaminants. Ten grams of the plastic was placed in the peritoneal cavity of each dog, care being taken to distribute the plastic particles evenly throughout the abdomen. Three dogs were used for each plastic tested. Penicillin was administered daily for the first three postoperative days.

Fig. 1.—Nylon. Seven days after operation. Acute inflammatory reaction and dense adhesions.

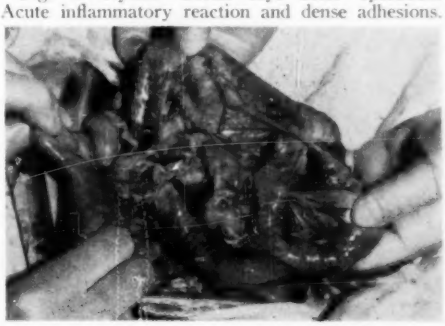

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Fig. 2.—Orlon. Seven days after operation. Acute inflammatory reaction and dense adhesions.

Fig. 3.—Dacron. Seven days after operation. Acute inflammatory reaction and dense adhesions.

Observations

Nylon.—All three dogs presented the same findings. There were numerous adhesions of bowel to bowel and some to parietal peritoneum. There was a moderate amount (150 cc.) of ascitic fluid. The plastic was well dispersed through the abdomen. Adhesions were very firm, and the serosa of the bowel tore when separated.

Microscopic Report: "The peritoneum reveals inflammatory change, with a few small strands of nylon incorporated in the immediately adjacent peritoneal tissues. The peritoneal surface is in part covered by exudate. This exudate is composed of rather compact fibrin intermingled with neutrophils, mesothelial cells, and some lymphoid cells."

Orlon.—All three dogs presented the same findings. There were numerous firm adhesions of bowel to bowel and bowel to omentum. These adhesions were separated with difficulty. A small amount of free fluid (50 cc.) was present.

Microscopic Report: "In areas there is considerable increase in fibrous connective tissue, and there are present some foreign-body giant cells. Reticuloendothelial cells are moderately numerous, and there are a few indeterminate cells, possibly young connective tissue cells. There is a definite fibroblastic reaction, as well as a foreign-body reaction."

Dacron.—All three dogs presented the same findings. There were many filmy adhesions of bowel to bowel and bowel to omentum. A moderate amount (100 cc.) of serosanguineous fluid was present. The Dacron in most instances was adherent to mesentery or bowel only by fibrinous exudate.

Microscopic Report: "There are present numerous small spaces surrounded by a foreign-body type of reaction, with foreign-

Fig. 4.—Teflon. Seven days after operation. Very little inflammatory reaction and only a few filmy adhesions.

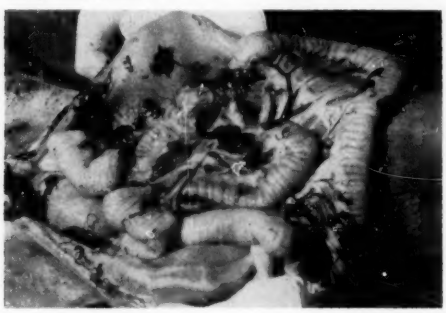

Fig. 5.—Marlex. Seven days after operation. Very little inflammatory reaction and no adhesions. Most of the pellets lay free in the peritoneal cavity; a few were encased in omentum.

body giant cells present in some places, which are more conspicuous than usual. The immediately adjacent tissue is edematous and reveals the presence of some fibrin. There is an increase in proliferation of young fibroblasts, but this is relatively inconspicuous in these sections."

Teflon.—All three dogs presented the same findings. There were a few filmy adhesions, bowel to bowel and bowel to omentum. These were easily separated. Much of the bowel and mesentery was covered with Teflon particles with no adhesions. There was no free fluid.

Microscopic Report: "Most of the Teflon is on or close to the surface of the peritoneum. There are present a moderate number of foreign-body giant cells in this immediate vicinity. There are a few dilated blood vessels filled with blood, and where this material (Teflon) is in the tissue, it is not surrounded by any reaction. The inflammatory change is largely limited to the surface."

Marlex.—All three dogs presented the same findings. There were no adhesions. Pellets of Marlex lay free in the peritoneal cavity. The omentum encased a number of the pellets, but only by filmy adhesions. None of the pellets were adherent to bowel, mesentery, liver, or other organs. About 100 cc. of free fluid was present in the abdomen. There was considerably less gross reaction seen than with nylon, Orlon, Dacron, or Teflon.

Microscopic Report: "The Marlex pellets have fallen out, but the area which they occupied is now irregular in shape and is lined by flat cells which suggest reticuloendothelial cells or cells of the peritoneum. Immediately adjacent there are cells apparently forming fibroblasts. The cells are elongated and suggest young connective tissue cells. The cytoplasm of some of these is vacuolated. Relatively little inflammatory change is present."

Summary

Both Teflon and Marlex showed considerably less foreign-body reaction than did nylon, Orlon, and Dacron, when implanted in the peritoneal cavity of dogs. Because it is well tolerated in tissues, and because of its desirable physical properties, Marlex would appear to be a valuable plastic for the fabrication of surgical prostheses.

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Case Reports

Gangrene of Gallbladder with Shock from Intraperitoneal Hemorrhage

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Recent reports [1,2] have emphasized the rare occurrence of gross intraperitoneal hemorrhage with gangrene of the gallbladder. We wish to report an instance of this kind and to summarize certain aspects of this entity on the basis of a study of all available reports of this condition.

Report of Case

A 54-year-old housewife was admitted to the hospital at midnight because of severe abdominal pain localized to the right upper quadrant, of 48 hours' duration. The patient had been given two injections of morphine while at home. Attacks of right upper quadrant pain had occurred at intervals during the preceding five years.

The oral temperature was 97.6 F (36.4 C); the pulse rate was 96 per minute; respirations were 22 per minute, and the blood pressure was 110/80 mm. Hg. Abdominal tenderness and rigidity were severe in the right upper quadrant, and 100 mg. of meperidine (Demerol) hydrochloride was given promptly for relief of pain. The white blood cell count was 23,000 per cubic millimeter and the hemoglobin level was 12.5 gm. per 100 cc. on admission. A diagnosis of acute cholecystitis was made, and conservative therapy was provided. When, within 10 hours, the patient appeared worse instead of better, operative intervention was recommended.

While preparations were being made for operation, shock developed; the blood pressure fell to 60/20 mm. Hg, and the pulse rate rose to 120 per minute. After transfusion of whole blood and oxygen therapy were begun, the condition of the patient improved. A combination of light general anesthesia with regional anesthesia, using 1% procaine hydrochloride, was employed. When the abdomen was opened, a large quantity of blood, both fluid and clotted, was found. This was cleared away.

When the gallbladder area was exposed, the distal half of the gallbladder was found to be missing. It had apparently been gangrenous and had "melted away," as not even shreds of tissue of this portion of the gallbladder were found. Digital examination of the remaining portion of the gallbladder disclosed a gallstone impacted in its lumen near the junction with the cystic duct. This was removed.

The remaining gallbladder wall was edematous and thick. The bleeding was from the branches of the cystic artery; blood was found spurting from each branch, as shown in the Figure. The bleeding points were ligated, and a section of the edge of the gallbladder wall was excised for biopsy purposes. Because of the general condition of the patient, and the edema which obscured the region of the cystic and common ducts, cholecystostomy was chosen as the safest procedure. A firm rubber drain was sewed into the remaining portion of the gallbladder. Two Penrose drains were inserted: One, placed just medial to the gallbladder, was brought out in the epigastric region. The other was placed in the region of Morison's pouch and was brought out laterally. The blood had been evacuated as completely as possible, and the abdomen was closed.

As the operation was finished and after 300 cc. of blood had been given, the blood pressure was 85/40 mm. Hg; the pulse rate was 120 per minute. The blood pressure soon rose to 120/80 mm. Hg, and 12 hours later the blood pressure was 190/90 mm. It remained in this general range for the following three days. It then dropped to approximately 120/80 mm. Hg, where it remained during the rest of the hospital stay. On the first postoperative day, the erythrocyte count was 4,400,000 per cubic millimeter, and 14 gm. of hemoglobin per 100 cc. of blood was present; the white blood cell count at this time was 11,400 per cubic millimeter. Streptomycin and penicillin had been given as part of the postoperative treatment.

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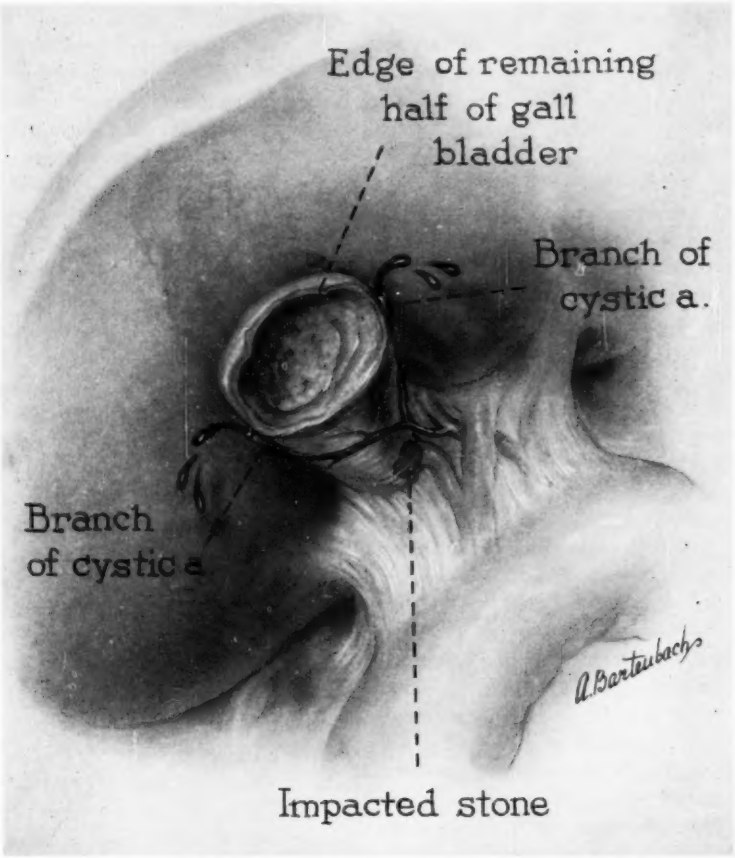

The area of gangrene and the source of the hemorrhage are depicted in this drawing. About one-half of the gallbladder remains. The distal portion had "melted away." Blood spurted from the branches of the right cystic artery, as shown. The stone was tightly impacted.

The blood recovered from the peritoneal cavity had a hematocrit reading of 37%; its specific gravity was 1.033, and its erythrocyte count was 3,510,000 per cubic millimeter. It contained 11 gm. of hemoglobin per 100 cc. of blood. A direct smear of this blood showed no bacteria. Escherichia coli organisms were isolated by culture. The biopsy of the gallbladder wall showed only granulation tissue.

The postoperative course was uneventful except for a febrile reaction. On the 13th postoperative day, a few hours after the withdrawal of one of the drains, the patient's temperature was 103.3 F (39.6 C). Some drainage was noted for a few days thereafter, but the temperature remained normal after the 15th postoperative day.

An oral cholecystogram made six months later failed to demonstrate a gallbladder shadow. A rounded opacity in the midabdominal area was seen on three of the cholecystographic films and may, in the opinion of the roentgenologist, have represented a gallstone. One could very well have escaped from the gallbladder and eluded discovery at operation. A recent report from the patient's personal physician states that she is in good general health, is having no symptoms of gallbladder disease, and is taking an unrestricted diet.

Comment

Gangrene and perforation of the gallbladder have been reported [3,4] in about 1% of all patients operated upon for gallbladder disease. In two large collected series an incidence of gallbladder perforations of about 12% has been reported in patients with acute cholecystitis.[3,5] However, if

chronic fistulas and subacute perforations with pericholecystic abscess are eliminated, perforation into the free peritoneal cavity occurs in about 1% of patients with acute cholecystitis.[4,6,7]

From a review of the literature,[1,2,8-25] our patient appears to be the 25th recorded case with intraperitoneal hemorrhage from a perforated or gangrenous gallbladder. With the exception of Fitts and coworkers,[21] who reported two cases in 1951, and Erfors and Örndahl,[25] who reported four cases in 1954, authors have as a rule reported single cases.

Involved in the 25 cases were 13 men and 12 women, with an average age of 61 and 62.5 years, respectively. The range for men was from 22 to 85 years and for women from 52 to 72 years. The greatest incidence for both men and women was in the seventh decade (four men and six women).

Fifteen of the twenty-five patients had had previous abdominal symptoms of some kind for varying periods of time. Only one report stated that the patient had previously been well; nine reports did not mention the patient's health before the onset of this acute illness. The duration of the acute episode associated with hemorrhage ranged from a few hours to a few days. Only five patients had acute symptoms longer than four days prior to operation or death.

Howard and associates[22] made the only correct preoperative diagnosis. The diagnosis made in most of the cases before operation was some acute abdominal catastrophe, signifying the urgency and severity of the symptoms. A "shock-like" picture was rarely emphasized. The diagnosis was made on postmortem examination in the six cases in which no operation was done.

Nineteen patients were treated by surgical operation performed as an emergency measure. Five of these patients died. Nine patients were treated by cholecystectomy, and all survived. Ten patients were treated by some kind of drainage procedure. Five of these patients survived.

Of the last 13 patients reported on, there have been 10 survivors. One death was the result of a coronary occlusion in the early postoperative period; another was in an 85-year-old man who was moribund on admission and died soon thereafter. The other death was in a 65-year-old man who had extensive peritonitis associated with the hemorrhage.

Three different sites of massive bleeding associated with perforation of the gallbladder have been reported. The vessels in the gallbladder wall at the site of the perforation (presumably due to acute cholecystitis) have been the source of the hemorrhage in 14 of the reported cases. In four patients the blood that escaped into the peritoneal cavity through a perforation in the gallbladder wall was found to originate at an independent area of ulceration in the mucosa, with erosion of vessels. Perforations of the gallbladder which have occurred close to or into the liver have caused lacerations of the liver, with hemorrhage from this site in three patients.

In any patient whose symptoms and findings are those of acute cholecystitis and in whom shock develops, perforation of the gallbladder should be suspected. If, in addition, there are indications of hemorrhage, the gallbladder can logically be suspected as the source. Prompt and intensive supportive therapy by transfusion of whole blood and early surgical intervention can be expected to result in a high percentage of survivors.

Summary

A case report of a patient who had massive intraperitoneal hemorrhage and shock as a result of perforation and gangrene of the gallbladder is presented. Only 24 similar instances could be found in the literature. A brief discussion of the pertinent findings in these cases is presented. Vigorous resuscitative measures, prompt operation, and an awareness of this possible cause of massive hemoperitoneum have resulted in a high percentage of survivors. Ten of the last

thirteen patients managed in this manner have recovered.

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Volvulus and Massive Gangrene with Survival

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Report of Case

A 25-year-old Persian villager was admitted to the American Christian Hospital at 8:45 a. m. on May 29, 1950. He had come by bus a distance of 60 kilometers, from his village. His chief complaint was severe abdominal pain. The pain was of 24 hours' duration, gradual onset, and cramping character and was generalized over the entire abdomen. With the passage of time the pain had become progressively severer. The patient had vomited several times and had had one bowel movement on the day prior to admission. He had been in good health before the onset of his present illness. He was in shock and in excruciating pain, thus being unable to give a detailed history.

On examination the physical findings were as follows: temperature 95.4 F; pulse 96 a minute; blood pressure 0. The patient was a well-developed and well-nourished man, appearing of about the stated age. He was dehydrated and in great pain and discomfort. His body was cold but dry. The respirations were rapid, shallow, and grunting in character. There were no enlarged lymph nodes. His eyes, nose, and throat were essentially normal. His chest was resonant to percussion, and there were a few fine crepitant rales at the base of the left lung and over the midportion of the right lung. The area of cardiac dullness was not enlarged. The pulse was 96 per minute and irregular, weak, and thready. The heart sounds were distant, and a systolic murmur was heard in the aortic area. The blood pressure was not obtainable. His abdomen was very tender, the most acute tenderness being over the right side. There was generalized abdominal rigidity, which was severer over the right side of the abdomen. There was no peristalsis. The area of liver dullness was mildly tympanitic and the abdomen moderately distended. The genitalia were normal, as was examination of the rectum.

This patient was obviously an acute abdominal emergency in serious condition. The signs and symptoms were typical of a relatively common condition seen in northwestern Iran, that is, volvulus of the intestine with gangrene.

Submitted for publication Dec. 26, 1957.

American Christian Hospital.

The patient was hospitalized and prepared for operation. An injection of morphine was given, and intravenous fluids and Wangensteen suction were started. By 10:30 a. m. his blood pressure had risen to 110/80, and he was taken to the operating room for surgery. Preoperative urinalysis revealed albumin 2+ and glucose negative. Microscopic examination showed many hyaline casts and very rare erythrocytes. His hemoglobin was 90% (13 gm.), and his leukocyte count was 14,240 per cubic millimeter. He had received 1000 cc. of 5% dextrose in saline by 10:30 a.m. The operation was begun after the abdominal wall was infiltrated with 0.5% procaine hydrochloride solution containing epinephrine to delay absorption.

The abdomen was opened through a right paramedian incision. When the peritoneum was opened, a dark, serosanguineous fluid and a loop of gangrenous intestine were seen. Further exploration revealed that a large portion of the ileum and the sigmoid colon were involved, separately, in a volvulus which had cut off the blood supply and caused gangrene of both. In addition, the two twisted loops had secondarily twisted around each other and the combined twist had herniated through the opening formed posteriorly by the intestine, its mesenteries, and the posterior body wall. The volvulus was reduced with considerable difficulty, and it was only after reduction that the complex combination of twistings could be understood.

The patient's condition remained fair during the operation. The distal segment of viable large intestine was too short to reach the abdominal wall. It was decided to exteriorize the gangrenous loops of intestine and perform an anastomosis between the proximal ileum and the rectum. This was done after sectioning the ileum several inches proximal to the sharply demarcated gangrenous portion and the rectosigmoid distal to the same. The point of section in each case was normal in color and appeared to have a good blood supply, as demonstrated by free bleeding of bright red blood on section. The rectosigmoid was closed with two layers of No. 40 cotton sutures, after which the anastomosis was done a few inches above the pelvic floor.

The gangrenous sigmoid was exteriorized through a stab wound in the left lower quadrant.

The ileum was exteriorized through a similar stab wound in the right lower quadrant, after mobilizing the cecum and ascending colon sufficiently to exteriorize the proximal few inches. The necrosis had extended to within ½ in. of the ileocecal valve, and it was not felt safe to attempt a closure here. Adult ascarides were found in the small intestine. Sterile sulfanilamide crystals, 5 gm., and dihydrostreptomycin sulfate, 1 gm., in sterile isotonic saline were placed in the peritoneal cavity, and the abdomen was closed without drainage. One-half hour after the operation was begun the blood pressure had dropped to 95/80. The only agents available to maintain blood pressure were dextrose and saline solution of local manufacture and ephedrine and epinephrine.

One hour after the operation had been started the blood pressure had dropped to 82/70 and remained there throughout the balance of the operation. The operation was completed at 12 noon, at which time his pulse had risen to 120 and his respirations were 48 per minute. Intravenous fluids were continued after the operation.

There were no congenital anomalies, no fibrous bands or adhesions, and no tumors, and the patient had never had a laparotomy.

Postoperatively morphine was given for sedation, and penicillin and dihydrostreptomycin were given to combat infection. The blood pressure was taken at frequent intervals. It ranged from 78 to 90 systolic until 5 p. m. Soon thereafter it began dropping, in spite of intravenous fluids, and at 5:30 p. m. it was unobtainable and the patient was in a cold sweat. He responded to ephedrine. He had no family able to donate blood, but a member of the foreign colony donated 500 cc. The transfusion was begun at 6:45 p. m., and no reaction ensued. His blood pressure was taken at frequent intervals and ranged from 78 to 100 systolic throughout the night and the next day. The parenteral fluids were continued on the first postoperative day, some being given by hypodermoclysis because this method resulted in fewer pyrogenic reactions. The exteriorized gangrenous bowel was removed and measured. There were 2 ft. of large intestine and 5 ft. of small intestine.

During the night of May 30 the patient had three watery bowel movements, and his urinary output was 1150 cc. in the first 24 hours. On the second postoperative day, his blood pressure stabilized at 110 systolic, and he had 25 watery bowel movements, containing three roundworms. His urinary output on that day was 700 cc.

He was given water by mouth frequently and in small amounts to help maintain hydration. No commercial parenteral fluids were available, and the solutions prepared in our hospital frequently gave pyrogenic reactions because of a defective still. His hemoglobin was 104% (15.1 gm.) and his leukocyte count 5760 per cubic millimeter. During the next two days his urinary output was fair, and his bowel movements continued to be copious. His hemoglobin dropped to 82% (11.9 gm.). His blood pressure remained good. On the fifth day a foul-smelling discharge developed from the wounds.

On the evening of the sixth day (June 4), he again had severe abdominal pain. Examination revealed the cecum to be no longer viable. The patient was reoperated upon, under local anesthesia. The anastomosis had broken down, and the cecum and part of the ascending colon had become necrotic, owing to poor blood supply. The patient had a pool of liquid feces in the pelvis. The stump of the ileum was again resected and anastomosed this time to the transverse colon. The cecum and part of the ascending colon were resected, with inversion of the stump. The defect in the rectum was closed. Miraculously, the patient survived the procedure. Our inadequate set-up for maintaining fluid and electrolyte balance made it necessary to be very bold surgically.

Postoperatively, antibiotics and vitamins were continued, and continuous Wangensteen suction was used. The systolic blood pressure ranged from 70 to 90 mm. Hg during the first 24 hours postoperatively. Isotonic saline solution was given parenterally throughout this period. On the second postoperative day, in addition to parenteral fluids, a transfusion of 750 cc. of citrated blood was given, with the result that his systolic blood pressure rose and remained above 100 mm. Hg thereafter. On the third day 300 cc. of citrated blood and more parenteral fluids were given. The colostomy began to discharge feces. His blood cell count was as follows: hemoglobin, 62% (9 gm.); red blood cell count 2,900,000; leukocyte count 7000, and differential count, 80% polymorphonuclear leukocytes, 17% lymphocytes, and 3% monocytes.

Iron therapy for his anemia was then begun. No further donors for blood could be found. On the fourth, fifth, and sixth days after operation his condition remained fairly good and the colostomy was functioning well. On the seventh day, however, it was noted that the upper end of the laparotomy wound was becoming necrotic and fecal material was coming from the wound at that point. Apparently, the anastomosis was leaking. The wound continued to discharge feces, but the colostomy was functioning well. The following day Ascaris lumbricoides worms began coming from the abdominal wound. The patient was losing weight, but the colostomy continued to function well, even though the wound drained profusely. The patient was maintained by parenteral

isotonic saline solution, in addition to his oral intake. Since fluids administered subcutaneously gave fewer pyrogenic reactions than by intravenous administration, the former route was used to a large extent.

On June 23 the fistula tract itself was first identified in the upper angle of the wound. On the same day the patient began to have bowel movements from the rectum again. It was thought that the stump of the ascending colon had sloughed out and a transperitoneal tract had formed connecting with the former site of anastomosis of the rectosigmoid, which apparently had not healed. The abdominal wound was developing granulations by this time. The patient had been running an irregular febrile course, but there had not been as great a febrile reaction as was anticipated from the appearance of the wound and the patient. On June 29 dihydrostreptomycin was discontinued. During the remainder of his hospitalization there was no further fever of note.

Parenteral fluids were discontinued on July 2. A complete blood count three days later showed hemoglobin 65% (9.4 gm.), and a red blood cell count of 2,820,000, with normal leukocyte and differential counts. His urinary output was maintained between 1000 and 1500 cc. a day by oral fluids. The fistula continued to discharge copiously, but the abdominal wound was gradually granulating in. He continued to have occasional bowel movements by rectum until July 17. His nutritional status had gradually deteriorated, until on July 17 his weight was only 90 lb. We had no record of his original weight, but he had been well nourished on admission and was a man about 5 ft. 6 in. in height. He now appeared almost cachectic.

On July 24 his hemoglobin was still quite low, but he was beginning to make some gain. By August 10 he had gained 5 lb. in weight, and on Aug. 14 his hemoglobin had risen to 85% (12.3 gm.). On August 24 the small-bowel fistula was closed under spinal anesthesia. Many loops of small intestine were involved in extensive adhesions, which were not disturbed, since there was no evidence of obstruction. Antibiotics and parenteral fluids were given postoperatively. He had a very smooth postoperative course except for slow healing of the abdominal wound. The colostomy continued to function well. Vitamins and ferrous sulfate were continued.

On Sept. 17 preparation of the colon for closure of the colostomy was begun, using sulfaguanidine 15 gm. daily in divided doses. On Sept. 18, his hemoglobin was 72% (10.4 gm.), but no blood was available for transfusion to prepare him for his last operation. Five days later, under continuous spinal anesthesia, the colostomy was taken down and the end of the descending colon was anastomosed to the rectosigmoid. All the organs were matted together in the pelvis in a dense mass of adhesions, making identification of the various organs and structures virtually impossible.

After considerable exploration the rectum was found, and an end-to-end anastomosis was performed. Postoperatively, antibiotics and Wangensteen suction were used. On the third postoperative day the patient had one loose bowel movement, and on the following day four movements. Thereafter his bowel movements were normal and regular. His postoperative course was smooth, and he made a good convalescence, being discharged from the hospital on Oct. 12, 1950, on the 19th day after his last operation. At this time his abdominal wounds were completely healed; he was having normal bowel movements and was completely free from pain. He was thin and somewhat anemic but otherwise in good condition. About four or five months later, and again after one year, he returned to our clinic from his village to bring his mother for treatment of trachoma. He had gained weight; his color was good, and he was and had been symptom-free. Thus ends the chapter of our first surviving case of massive gangrene of the intestine due to volvulus. Perhaps at a later date time will permit the reporting of our experience with a series of these cases.

Summary

The case of a 25-year-old Persian man operated upon for volvulus with gangrene of the ileum and sigmoid colon simultaneously with survival is reviewed. A segment of 2 ft. of large intestine and 5 ft. of small intestine was exteriorized and later removed because of the gangrene. There were many postoperative complications, some of which related to the lack of adequate blood and satisfactory solutions for parenteral administration. The patient was discharged 136 days after admission to the hospital symptom-free, and follow-up for one year showed him to be in good health.

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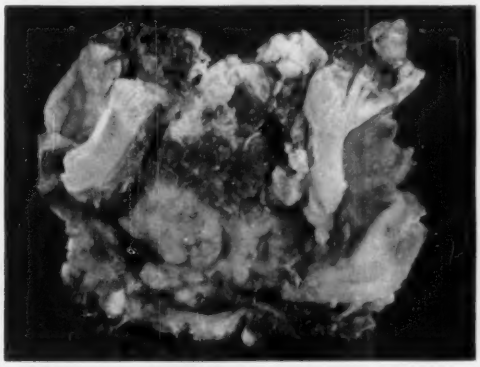

Figure 2 *(above)*—Photograph of a portion of the resected synovium with attached menisci from the case shown in Figure 1. Note the deep brownish color of parts of the villously hypertrophied synovium.

Figure 1 *(above)*—Lateral radiograph of knee area in a case of pigmented villonodular synovitis in a man of 53 years. Note the lobulated soft-tissue masses posteriorly and the effects of invasion of the patella and the femoral condyles by lesional tissue.

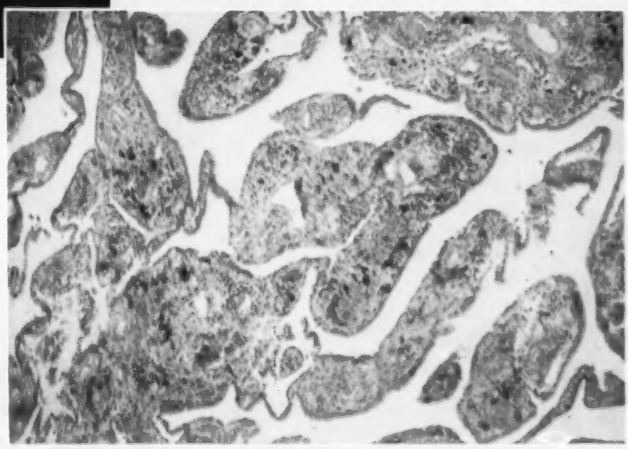

Figure 3 *(right)*—Photomicrograph (x 25) showing a tissue area in a villonodular synovitis in which the proliferated villi are matted together. The brownish discoloration of the tissue is due to hemosiderin pigment.

Turn page for data on Synovial Osteochondromatosis . . . 3 aspects

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Figure 1 *(above)*—A lateral radiograph from a case of synovial osteochondromatosis of the knee. Note the faint opacities in the suprapatellar pouch area and in the posterior compartment.

Figure 2 *(above)*—Photograph showing the synovial surface of the suprapatellar pouch. Note the cartilaginous excrescences, many of which are protruding from the surface.

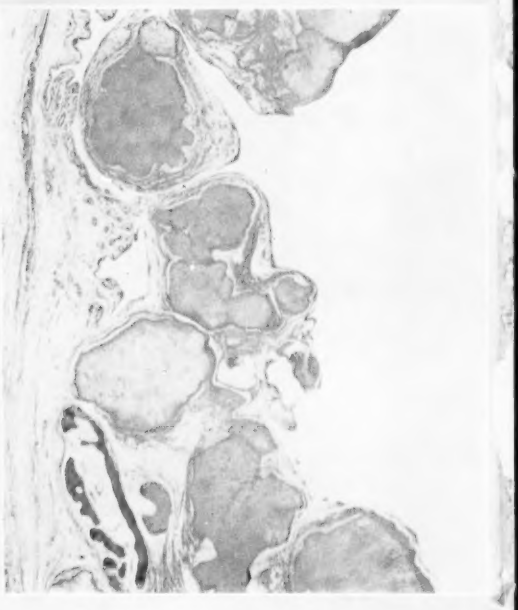

Figure 3 *(right)*—Photomicrograph (x 3) of representative section prepared from lesional tissue shown in Figure 2. Note the numerous islands of cartilage within the synovial membrane. Some are agglomerated and are protruding into the pouch.

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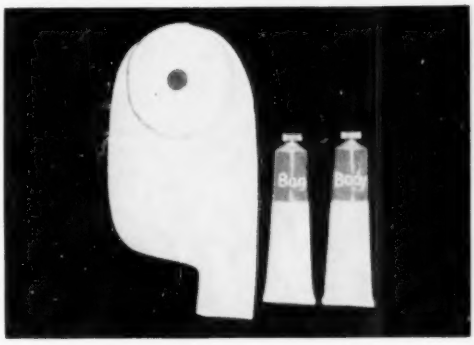

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Jordan and Grossman; Arch. Surg. 74: 871, 1957
Shingleton, et al; Surgery, 42: 12, 1957
Longmire, Jordan and Briggs; Ann. Surg. 144: 681, 1956
Krane; Am. Pract. and Digest, 8: 1275, 1957

Literature on request.

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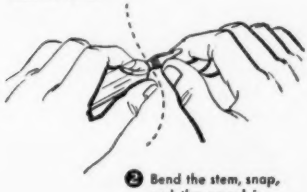

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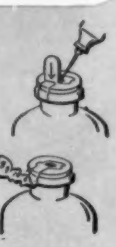

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